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CLINIC OF DR. GEORGE R. MINOT

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A NON-FATAL CASE SIMULATING ACUTE LEUKEMIA WITH ANEMIA AND THROMBOPENIC PURPURA

CONFUSION between acute leukemia and infectious mononucleosis occurs rather frequently, although usually it should not be difficult to distinguish the one condition from the other. Acute leukemia is a rapidly fatal disease, whereas patients with infectious mononucleosis recover. There is no particular sort of treatment that influences importantly either of these conditions. It is desirable, however, to make a correct diagnosis and to not offer an incorrect prognosis.

The occurrence of distinct anemia and purpura, associated with very few blood platelets (thrombopenia), is considered not to occur, or at least to be very rare, in infectious mononucleosis, but both conditions are features of acute leukemia. Eight years ago the patient I am to show you had both pronounced anemia and thrombopenia, and yet he has remained well since then. Hence, it is difficult to believe that he suffered from leukemia unless one admits that he recovered from a condition supposed to be fatal. Whether the case should be considered as related to the condition known as infectious mononucleosis, or whether it should be classified as a peculiar form of idiopathic purpura hemorrhagica (idiopathic thrombopenic purpura), or as a separate type of condition, is open to question. The important point for you to recognize is the similarity of this case to cases of acute leukemia and that it illustrates an instance of where a patient's

condition appeared to indicate a rapidly fatal issue and yet recovery soon took place.

Eight years ago at the age of eighteen years this young man, who appears today perfectly well, experienced during the months of August and September abnormal fatigue. During this period of time he was "restless and cranky" and constantly felt "out of sorts." He became progressively and rapidly weaker during the first two weeks of October and noticed shortness of breath on exertion, palpitation of the heart, and increasing pallor. He also had for about five days mild diarrhea. On October 10th purpura appeared about the elbows and neck, and bleeding from the gums and nose soon followed and continued for about a week.

The patient was seen on October 15th, when he appeared distinctly sick, pale, and underweight. Height 5 feet 8 inches. Weight, 110 pounds. This was about 6 pounds less than he weighed two months previously. Temperature 100.5° F. Pulse rate, 90 per minute. Respiration rate, 22 per minute.

The skin presented many purpuric lesions. There were many fresh and old petechiæ above both clavicles, on the lower legs, and about the elbows. Similar lesions were distributed sparsely over the face, arms, and anterior aspect of the trunk. Several large diffuse superficial ecchymoses were present on both thighs and outer aspects of the right forearm. A subconjunctival hemorrhage occurred in the right eye. The gums oozed a little blood and petechiæ existed in the mucosa of the mouth. There was no evidence of bleeding from the gastro-intestinal tract and the stool gave a negative test for occult blood. The urine, however, contained a few red blood-cells and a slight trace of albumin.

The tonsils were slightly enlarged and showed signs of chronic infection. Many lymph nodes on both sides of the neck were obviously enlarged, the largest (about 8 on each side) being about 4 x 4 cm. They were discrete, soft, and not tender. Similar sized nodes occurred in the axillæ and many lymph-nodes larger than normal were in the groins. The epitrochlear lymph-nodes were palpable, but very small in size. No other lymph-nodes were felt elsewhere than noted. The spleen descended on ordi-

nary inspiration about 5 cm. below the costal margin. The liver was not palpable. Examination of the abdomen was otherwise negative. The lungs presented no abnormality nor was there evidence on physical examination of mediastinal disease. No Roentgen-ray examination was made, however, to determine whether or not enlarged lymph-nodes existed within the thorax. The heart was normal. There was a functional soft systolic murmur localized at the pulmonic area. Other aspects of the physical examination were negative.

Questions brought forth the following additional information that might be considered to have a bearing on the case. There had been a few palpable lymph-nodes in the neck for two years, but the patient was certain that they had increased in size and number in the preceding two weeks. The boy had experienced several attacks of tonsillitis, although he had not had an attack for over a year. Probably a small part of the enlargement of the lymph-nodes in the neck was due to chronic infection of the tonsils.

The patient had been always abnormally thin and "cranky and fussy about his food." He disliked many sorts of green vegetables, milk, eggs, and butter, but enjoyed all forms of fish, meat, poultry, fruit, and cereals. His diet, however, had been of a sort that permitted scurvy to be excluded as the diagnosis. He grew unusually rapidly in height during his sixteenth year of life. Apparently he had been considered always a "delicate boy" with a "nervous, jumpy, irritable temperament."

Measles and whooping-cough were the only specific diseases he had had. No one of his three brothers nor any of his relatives or friends were known to have had any disorder of the blood or lymphoid tissue.

The blood showed as follows:

Hemoglobin 55 per cent. (Sahli).

Red blood-cells 3,300,000 per cu. mm. They were somewhat achromic, varied moderately in size and only a little in shape. Microcytes were not present. About 1 per cent. of the cells were polychromatophilic and 4 per cent. were reticulocytes.

The *blood platelets* were reduced to about 25,000 per cu. mm.

The *blood clotted* in normal time, but the clot was soft and friable and did not retract even after being kept at body temperature for twenty-four hours.

The *serum* was not abnormal in color, suggesting that it contained no excess of pigments. It yielded a negative Wassermann reaction.

The white blood-cells were 12,000 per cu. mm.

A differential count of 400 cells showed as follows:

	Per cent.
Polynuclear neutrophils of normal types	15
Small lymphocytes of normal types	6
Pathologic lymphocytic cells	75
Typical monocytes	4
	100

No polynuclear eosinophils or basophils were seen.

It is not my purpose to discuss the detailed histologic features of the abnormal cells that occurred in this patient's blood and their distinction from various other types of cells. This sort of knowledge you can obtain satisfactorily only by a study of preparations of blood. The colored plates in the following articles will help you to appreciate the character of the cells that occur in the blood of acute leukemia and of infectious mononucleosis.

1. Downey, H.: The Myeloblast, Its Occurrence under Normal and Pathologic Conditions, and Its Relations to Lymphocytes and Other Blood-cells, Folia Haematologica, 1927, 34, 145.
2. Downey, H., and McKinlay, C. A.: Acute Lymphadenosis Compared with Acute Lymphatic Leukemia, Archives of Internal Medicine, 1923, 34, 82.
3. Baldridge, C. W., Rohner, F. J., and Hanemann, G. H.: Glandular Fever (Infectious Mononucleosis), Archives of Internal Medicine, 1926, 38, 413.
4. Panton, P. H., Tidy, H. L., and Pearson, G. H.: The Leukemias: An Anlaysis of Fifty-nine Consecutive Cases, The Quarterly Journal of Medicine, 1914, 7, 340.

5. Minot, G. R., and Smith, L. W.: The Blood in Tetrachlorethane Poisoning, Archives of Internal Medicine, 1921, 28, 687.

A paper by Schenck and Pepper entitled, "Concerning the confusion between acute leukemia and infectious mononucleosis; with the report of a case of acute lymphoblastic leukemia with remission," appearing in the American Journal of the Medical Sciences, 1926, 171, 320, is among many others worthy of your attention.

A distinctive feature of the abnormal cells in acute leukemia, disregarding whether leukopenia or leukocytosis exists, is the pronounced immaturity of either all or at least the majority of the white blood-cells. This is detected particularly by the character of the inner structure of the nucleus, which will show nucleoli. In infectious mononucleosis markedly immature cells are rare and never more than a very small number of such cells have been recorded. With a little experience one can almost always readily distinguish the predominating cells found in infectious mononucleosis from those characteristic of acute leukemia and rarely will confusion arise. In the case of this boy many of the abnormal cells were most difficult to classify. Fifteen per cent. were considered slightly abnormal large lymphocytes. Sixty-five per cent. closely approached in character the type of cell found to predominate in acute leukemia and rarely observed in infectious mononucleosis. These cells were considered to be Downey's Type III[1] cells, cells that he found in one case of infectious mononucleosis. Some of the cells seemed even more immature than those shown in the plate that illustrates Downey's paper. Ten per cent. of the abnormal cells showed features characteristic of primitive grossly immature cells (lymphoblasts and myeloblasts). Such cells are not to be expected in infectious mononucleosis and are found in large numbers in acute leukemia. The remaining 10 per cent. of pathologic lymphocytic cells were certainly not immature and resembled different cells illustrated in the plate of Baldridge and associates' article referred to above.

This patient's white blood-cell picture did suggest that leu-

[1] Reference Number 2 loc. cit.

kemia might be the correct diagnosis. Cases of leukemia may show at no time a distinctly high white blood-cell count so that the level of the leukocytes does not determine whether or not leukemia is present. In acute leukemia, anemia that rapidly progresses to an extreme degree and a pronounced decrease of blood-platelets are features of the blood. Both these conditions occurred in the patient which further suggested that he had leukemia. His clinical history and the enlargement of his spleen and lymph-nodes and the purpura also were consistent with this diagnosis.

Four days after the patient was first seen his blood and general condition were essentially the same, except no new purpuric lesions had appeared, the urine contained no blood and the bleeding from the gums and nose had ceased. About two weeks later he was symptomatically very much better; the spleen was smaller but palpable and the lymph-nodes had decreased in size. The blood then showed as follows:

Hemoglobin 65 per cent. (Sahli).

Red blood-cells 3,800,000 per cu. mm.

The blood-platelets had increased to normal numbers and the blood-clot retracted in normal fashion.

The white blood-cells 10,200 per cu. mm.

A differential count of 400 cells showed:

	Per cent.
Polynuclear neutrophils	44.0
Polynuclear eosinophils	1.0
Polynuclear basophils	0.25
Lymphocytes—small	15.75
Pathologic lymphocytic cells	35.0
Monocytes	4.0
	100.00

None of the pathologic lymphocytic cells were grossly immature and only 20 per cent. resembled Downey's Type III cell. The majority were slightly atypical large lymphocytes.

The patient received no especial sort of treatment. He was kept in bed and given an ordinary well-balanced diet.

Circumstances prevented the patient being seen again until fourteen months had elapsed, during this interval his tonsils

were removed and he gained 17 pounds in weight. He then appeared well. His spleen was not palpable and only a few very small lymph-nodes were detected in his neck, axillæ, and groins. His blood was normal in all respects. Since that examination, about seven years ago, he has been perfectly well except for suffering from several mild upper respiratory infections.

Inasmuch as the disease acute leukemia is considered always fatal, one hesitates to state that the boy had this condition. Even so it is conceivable that he had leukemia. Is this case to be classed as an atypical one of infectious mononucleosis? If so one must recognize it presented very unusual features. Distinct anemia is at least very rare in infectious mononucleosis and its absence is considered usually of diagnostic importance. No records appear of cases of infectious mononucleosis with pronounced decrease of the blood-platelets while the occurrence of any hemorrhagic diathesis is distinctly unusual. Downey and McKinlay record that two of their cases showed hemorrhages into the mucosæ and skin, but they were not extensive or associated with distinct anemia. They do not mention the level of the blood-platelets in these 2 cases. I lay stress on the fact that thrombopenic purpura is common in acute leukemia but the purpuric skin lesions rarely become profuse, as occurred in this boy, until the hemoglobin has fallen below 50 per cent. or lower than it was in this patient. Furthermore, it is to be recalled that the white-cell picture was atypical for infectious mononucleosis and presented some leukemic features. Infectious mononucleosis almost always begins acutely and often with symptoms referable to infection of the throat and occasionally with symptoms referable to the gastro-intestinal tract. The onset of acute leukemia is relatively insidious and there is often a history of poor health for some weeks before serious symptoms develop, which is what occurred in this patient.

Mouth and throat lesions due to infection and often of a severe nature are common in leukemia, but these usually arise as the result of lowered resistance after the disease has existed some time. Such symptoms, however, may be the ones for which the leukemic patient first consults a physician. This young man

showed no signs of acute infection of the tonsils or throat, although chronic infection of the tonsils was present.

There is nothing distinctive concerning the lymph-node or splenic enlargement to undoubtedly differentiate the two conditions, but there is a greater tendency for the adenopathy to be limited in infectious mononucleosis to the cervical and submaxillary lymph-nodes and for individual nodes to be largest in leukemia.

Conditions associated with an absolute or relative lymphocytosis composed of normal lymphocytes can be excluded as having existed in this patient. Cases of the condition known as agranulocytic angina may be confused at times with those of infectious mononucleosis. This condition of angina with leukopenia and with a relative lymphocytosis has been reviewed carefully by Kastlin.[1] In this condition anemia is slight and the blood-platelets remain unaffected.

There is a condition in which the blood platelets become very few with ensuing purpura and hemorrhages from the mucosæ and later anemia and yet rapid recovery may occur. This is acute idiopathic purpura hemorrhagica. Patients with this condition who recover usually show definite signs of improvement within three weeks after the onset of purpura. The spleen rarely may become palpable. These features of idiopathic purpura hemorrhagica were present in the case of this patient but such enlargement of lymph-nodes as occurred, is not associated with the condition, nor was the white cell blood-picture like that of this hemorrhagic disorder. In idiopathic purpura hemorrhagica the white blood-cells usually number about 12,000 per cu. mm. I have observed the polynuclear neutrophils may not be increased and there may develop a lymphocytosis as high as 60 per cent., but when this has occurred the majority of the lymphocytes have been of normal types. I have never observed any such number of distinctly abnormal appearing cells as were found in the blood of this patient before you. I have seen in such cases a few lymphocytes that deviated slightly

[1] Kastlin, S. J.: Agranulocytic Angina, Amer. Jour. Med. Sci., 1927, 73, 799.

from normal and rarely have found a distinctly immature lymphocyte. Immature cells, however, derived from the bone-marrow are apt to occur in such cases. It is not unusual to observe a few, and rarely a considerable number, of myelocytes of different types. The blood-picture and lymph-node enlargement the patient had, does not permit one to record the case as one of idiopathic purpura hemorrhagica with recovery.

I cannot make a precise diagnosis, but the case was certainly an atypical one of unknown etiology that illustrates that severe injury to the hematopoietic tissues can take place and yet recovery occur. It further illustrates that to give a name to a morbid condition accomplishes but little in itself. Nosography, as Faber has pointed out, is one of the means that aids to our understanding disease, but our final aim is to acquire knowledge concerning etiology and concerning the consequent development and effect of the morbid process, so as to be able to apply proper corrective measures.

CONTRIBUTION BY DRS. ELLIOTT P. JOSLIN, HOWARD F. ROOT, PRISCILLA WHITE, W. STANLEY CURTIS, AND MR. H. D. ADAMS

NEW ENGLAND DEACONESS HOSPITAL

DIABETIC COMA

Contents:

Preamble.—Shall alkalies be employed in the treatment of diabetic coma? To answer this question for ourselves and for others who seek our advice, we here summarize 105 successive cases of coma, treated without alkalies, at the New England Deaconess Hospital between January, 1923 and February 1, 1929. On former occasions[1] we made reports of 33 and 30 cases

[1] Joslin, Root, White: Med. Clin. N. Amer., 1925, 8, 1873. Joslin, Root, White, Kiefer: Med. Clin. N. Amer., 1925, 8, 1921. Joslin, Root, White: Med. Clin. N. Amer., 1927, 10, 1281.

respectively, but from the former we have dropped nine[1] cases and from the latter two[2] cases, because, although strictly coma, the CO_2 volume per cent. in certain instances was taken after the administration of insulin or was considered from determinations of the CO_2 in the alveolar air to be 20 volumes per cent. or less which have been the criterion established for our diagnosis of coma. To the revised first series of 24 cases, the revised second series of 28 cases we now add a third series of 53 cases making the total of 105 instances of coma.

Results of Treatment Without Alkalies of 105 Cases of Diabetic Coma.—Two of the patients died of uncomplicated coma, but it is noteworthy that their fatalities were in 1923. Since that date there has been no death of a patient from uncomplicated coma under our care at the Deaconess Hospital. Five of the patients died during coma with complications. Seven cases recovered from coma, but died in the hospital after intervals of six to thirty-one days with complications. Autopsies were performed upon 10 of the 14 fatal cases. The remainder of the patients left the hospital alive, six have since died, and the balance were proved to be alive on March 1, 1929.

Here then is a list of one hundred and five diabetic comas, representing ninety individual patients, with fourteen deaths, two during uncomplicated coma treated in the early insulin period, five during coma with complications, and seven of complications after recovery from coma, and of the remaining patients all but six remain alive. In the face of these facts there appeared little reason for us to change our methods and to give alkalies. When we learned through the kindness of Professor Blackfan of the Children's Hospital that they had been still more fortunate and had treated successfully twenty-one instances of diabetic coma in succession and that of this number only one had received alkalies, we became all the more convinced of the soundness of our position.

[1] Case Numbers 1609, 2448 (two entrances for coma), 2687, 3129, 3859, 3877, 4033, 4279. Case Number 2801 was not omitted because on her third day after admission she relapsed into coma and her CO_2 was 17 per cent.

[2] Case Numbers 3040, 3456.

Therefore, we shall not give alkalies for diabetic coma in our clinic and this advice we shall continue to give other physicians until those who advocate alkalies report a comparable series of cases with better results than our own and as good as those of the Children's Hospital.

Deaths During Coma, During Complications After Recovery from Coma, and During a Subsequent Period, Varying Between One Month and Six Years.—The two patients, Case Numbers 3021 and 3240, who died of uncomplicated coma three and one-half hours and six hours after admission in 1923, we believe could have been saved if treated more energetically with insulin, caffein, and salt solution, and if lavage of the stomach had been earlier performed.

Of the 5 cases who died with complications during coma, autopsy upon Case 3267, dying two days after admission, showed an infectious pancreatitis with fat necrosis which was so extensive as to make surgical interference useless; autopsy upon Case Number 4525, who entered in a moribund state, dying twelve hours later disclosed peritonitis and septicemia from rupture of a labial carbuncle into the abdominal cavity; autopsy upon Case Number 6759 who entered the hospital in profound coma, CO_2 9 volumes per cent., and died within seven hours of admission, blood-sugar 0.70 per cent., non-protein nitrogen 70 mg. per 100 c.c., blood-pressure 30 mm. mercury in the right radial, revealed bronchopneumonia and multiple abscesses of the kidneys. Case Number 6893 died six hours after admission. She had active lues and may have had complications therefrom, but an autopsy was refused. She had less insulin and her salt solution and cardiac stimulation were given less promptly and efficiently than usual. Her change for the worse was sudden and unexpected. Case Number 7152 recovered from coma in the laboratory but not in the ward and died in extreme collapse. Possibly hyperthyroidism was a complication; no autopsy.

Autopsies upon three of these patients dying during coma demonstrated irremediable conditions. Two patients in 1923 died because of treatment which today we would consider

TABLE 1

53 Consecutive Cases of Diabetic Coma.

Case No.	Age at coma years.	Duration of D.M. years.	Date.	Clinical data.		Blood.									Urine.			Insulin.			
				Respiration.	Mental condition.	Sugar, per cent.			Plasma CO_2 combining power. Volumes per cent.			Non-protein nitrogen mg. per 100 c.c.			At entrance.		Sugar free after entrance hours.	Units.			
						Day.			Day.			Day.			Diacetic acid.	Sugar per cent.		Day.			
						1	2	3	1	2	3	1	2	3				1	2	3	
			1927																		
5929	31.5	0.6	Mar. 3	Kussmaul	Responsive	0.33	0.19	..	20	..	..	24	..	..	+++	5.0	13	135	25	30	
6082	51.7	5.9	May 16	Kussmaul	Unresponsive	0.57	0.28	0.16	13	20	23	154	145	125	0	trace	8	60	50	30	
3778	13.7	6.4	June 17	Kussmaul	Drowsy	0.30	0.30	..	16	27	..	38	..	..	++	0.5	9	60	40	40	
6159	44.4	1.2	June 23	Kussmaul	Unresponsive	0.84	0.36	0.24	9	31	39	63	38	31	+++	2.8	96	325	60	30	
6194	60.0	1.1	July 25	Kussmaul	Drowsy	0.42	0.17	0.36	15	16	34	53	47	42	+++	2.5	..	115	55	30	
3432	33.4	8.8	Aug. 1	Kussmaul	Unresponsive	0.66	0.19	0.27	9	31	54	53	34	..	++++	3.5	17	380	65	72	
2589	16.0	6.9	Aug. 6	Kussmaul	Drowsy	0.48	..	0.25	8	26	29	..	30	35	++++	2.7	19	165	35	35	
5042	13.6	1.9	Aug. 7	Kussmaul	Drowsy	0.61	0.44	0.37	16	32	39	77	57	47	+++	5.0	42	115	25	50	
3353	15.3	4.8	Aug. 28	Kussmaul	Stuporous	1.10	0.51	0.31	12	14	35	..	..	13	+	1.4	19	350	35	35	
5018	6.8	1.7	Sept. 9	Kussmaul	Responsive	0.38	0.32	0.36	9	14	30	17	21	28	++++	4.5	33	160	15	20	
4099	21.0	4.0	Sept. 18	Kussmaul	Unconscious	1.62	0.51	0.26	13	46	..	140	74	72	+	1.6	..	255	50	40	
3877	18.1	3.5	Oct. 1	Kussmaul	Drowsy	0.42	..	0.39	16	..	..	35	..	..	+++	2.3	60	100	65	55	
4535	40.2	2.8	Oct. 5	Kussmaul	Stuporous	0.47	0.16	..	5	21	..	..	30	..	++++	3.0	..	240	45	30	
6356	11.8	1.6	Oct. 10	Kussmaul	Unconscious	0.35	0.16	0.17	12	14	..	..	..	..	++++	4.8	25	105	50	30	
1616	14.1	8.4	Dec. 11	Kussmaul	Unresponsive	0.34	0.10	0.06	14	21	..	..	72	..	++++	3.2	10	40	65	40	
6511	50.0	2.0	Dec. 19	Kussmaul	Unresponsive	0.56	0.24	0.17	14	15	..	39	..	..	++	4.4	23	160	30	10	
2008	36.2	7.2	Dec. 21	Kussmaul	Responsive	0.36	0.09	0.08	15	39	..	51	32	..	++++	7.0	29	110	40	60	
5582	22.3	1.3	Dec. 21	Kussmaul	Unresponsive	0.70	0.11	..	17	32	..	61	..	..	++	2.8	18	215	40	45	
6522	24.9	1.5	Dec. 24	Kussmaul	Conscious	0.36	0.10	0.17	15	..	..	..	..	..	++++	1.0	12	80	50	45	
			1928																		
6033	22.0	0.7	Jan. 17	Kussmaul	Unresponsive	0.86	0.42	0.61	6	29	27	80	..	95	++++	3.9	..	440	40	45	
3729	29.5	5.0	Jan. 30	Kussmaul	Conscious	0.36	0.09	..	14	..	..	30	..	..	+++	2.5	..	85	40	30	
6287	12.5	5.7	Feb. 15	Normal	Drowsy	0.46	..	..	19	..	..	..	..	..	+++	4.5	14	60	25	40	
4600	64.1	8.0	Feb. 27	Kussmaul	Stuporous	0.70	0.13	..	12	..	..	80	64	..	+	2.5	28	250	20	40	
6729	50.0	14.0	Mar. 10	Kussmaul	Drowsy	0.78	0.80	0.30	8	..	45	48	..	32	++++	3.0	24	380	50	70	
6759	48.9	3.8	Mar. 30	Kussmaul	Unconscious	0.70	..	..	9	..	..	82	..	..	++	3.0	..	260			
4232	20.8	7.5	Apr. 3	Kussmaul	Responsive	0.29	..	..	14	..	..	..	..	..	+++	1.5	..	70	60	45	
6767	13.8	3.0	Apr. 22	Kussmaul	Responsive	0.36	0.08	..	15	38	..	43	..	..	+++	3.0	12	70	30	35	
6901	29.7	0.1	May 9	Normal	Conscious	0.43	0.15	..	19	..	..	..	..	..	++++	4.5	15	110	50	55	

4250	14.0	4.9	May 23	Kussmaul	Conscious	0.92	0.29	0.04	8	..	40	98	..	..	++	2.0	..	210	60	35
6920	47.1	3.5	May 27	Kussmaul	Drowsy	0.50	0.20	0.18	14	24	..	..	49	..	+++	3.5	69	145	45	40
6983	30.8	0.8	June 19	Kussmaul	Unconscious	1.04	..	..	10	..	..	80	..	..	++++	5.0	..	400		
7021	70.0	1.8	June 22	Kussmaul	Unconscious	0.74	0.11	0.48	6	..	..	62	..	..	+++	5.0	16	270	40	50
4312	49.0	6.1	July 28	Kussmaul	Stuporous	0.50	0.11	..	12	27	..	46	..	..	++	3.0	46	340	25	45
7152	51.2	0	Aug. 25	Kussmaul	Unconscious	0.72	0.32	..	13	25	..	70	56	..	+++	3.0	..	736		
2856	16.7	6.5	Aug. 28	Kussmaul	Drowsy	0.58	0.18	..	11	33	..	44	..	..	++++	2.8	15	205	50	55
6767	14.1	3.2	Aug. 31	Kussmaul	Stuporous	0.50	0.07	..	16	32	..	..	41	..	+	4.8	13	180	60	30
7234	16.0	0.8	Sept. 21	Kussmaul	Conscious	0.26	0.20	..	20	..	..	27	..	..	++++	3.6	9	75	25	20
7047	11.1	0.3	Sept. 27	Kussmaul	Unconscious	0.40	0.27	..	14	38	..	..	..	..	++++	4.2	21	70	40	30
6287	13.2	6.4	Oct. 23	Kussmaul	Drowsy	..	0.14	..	18	..	..	..	39	..	++	4.0	11	95	45	45
3682	14.8	6.0	Oct. 31	Kussmaul	Drowsy	0.29	0.15	..	13	27	..	..	47	..	+	1.0	7	65	40	50
6223	13.3	5.4	Nov. 7	Kussmaul	Conscious	0.31	0.05	..	20	41	..	..	35	..	++	0.2	9	80	25	15
7465	50.0	3.8	Nov. 21	Kussmaul	Drowsy	0.47	0.16	0.19	11	41	..	63	38	..	+++	2.6	36	170	25	30
6664	5.5	1.0	Dec. 6	Kussmaul	Conscious	0.36	0.17	0.12	15	20	..	42	35	..	++++	3.0	30	146	40	45
5692	11.2	2.1	Dec. 6	Kussmaul	Conscious	0.40	0.14	0.26	12	32	..	..	..	..	++++	1.4	10	95	12	24
3005	18.7	5.0	Dec. 31	Kussmaul	Conscious	0.45	0.08	0.11	18	40	53	..	45	35	+++	3.0	..	140	50	60
			1929																	
7486	33.0	7.0	Jan. 2	Kussmaul	Drowsy	0.54	0.13	..	11	28	..	45	..	..	++	2.5	..	250	50	70
7557	55.5	0.3	Jan. 5	Kussmaul	Conscious	0.74	0.12	..	10	22	..	65	..	..	++	4.2	17	450	5	15
2786	48.3	6.6	Jan. 5	Kussmaul	Conscious	0.59	0.11	..	9	33	..	..	..	..	+	2.8	16	120	30	30
6287	13.5	6.7	Jan. 9	Normal	Drowsy	0.20	0.14	..	20	31	..	..	32	..	++++	2.0	6	25	..	30
3391	41.3	6.5	Jan. 13	Kussmaul	Conscious	0.34	0.14	..	19	..	..	53	..	..	++	2.4	3	105	37	24
5724	8.0	2.4	Jan. 14	Kussmaul	Conscious	0.45	0.17	..	5	19	..	69	50	..	+++	4.8	30	105	30	35
1778	43.6	2.1	Jan. 25	Kussmaul	Stuporous	0.46	..	0.11	12	23	..	..	..	..	+++	4.4	..	210	40	30
7565	39.0	4.6	Jan. 28	Kussmaul	Conscious	0.19	0.18	..	19	26	..	41	42	..	++	0.8	..	85	50	35

inadequate, but whether there was sufficient excuse for the syphilitic, Case Number 6983, and for Case No. 7152 to die we are in doubt. The latter lived sixteen hours after treatment was started and made a chemical recovery though she never regained consciousness. This patient received alkali amounting to 30 gm. by mouth after her CO_2 had risen from 13 to 16 volumes per cent. She had a temperature of 104° F., and râles at the base of one lung. She had been given morphin before we saw her, appeared in profound shock, gave symptoms of tetany, but her blood calcium was 12 mg. per 100 c.c. In addition to 736 units of insulin she had one blood transfusion. She did not behave like the ordinary case of diabetic coma. No autopsy. One hour before death her blood-sugar was 0.32 per cent. and her CO_2 was 25 volumes per cent.

TABLE 2

SUMMARY TABLE—COMPARATIVE STUDY, BY AVERAGES, OF THE THREE SERIES

Series and number of cases.	Age at coma years.	Duration of D.M. years.	Date.	Blood.						Urine. At entrance.		Insulin. Units.		
				Sugar, per cent.		Plasma CO_2 combining power. Volumes, per cent.			Non-protein Nitrogen Mg. per 100 c.c.	Diacetic acid.	Sugar, per cent.			
				Day.		Day.			Day.			Day.		
				1	2	1	2	3	1			1	2	3
I 24 cases	31.5 24	2.4 24	May, 1923 to Mar., 1925	0.47 23	0.20 20	15 24	33 20	31 10	47 16	++++ 24	3.3 24	154 24	63 22	58 21
II 28 Cases	31.6 28	2.8 28	Apr., 1925 to Feb., 1927	0.49 28	0.20 20	14 28	29 20	30 10	46 21	+++ 28	3.4 28	166 28	59 25	49 [illegible]
III 53 Cases	29.1 53	4.0 53	Mar., 1927 to Feb., 1929	0.53 52	0.21 46	13 53	28 37	38 12	60 33	+++ 53	3.1 53	183 53	40 50	39 50

The small sub-figures indicate the number of determinations upon which the average is computed in each series.

The seven remaining deaths were of patients who completely recovered from coma, but died from other causes. Case Number 2988 entered with coma and pneumonia and died six days later in consequence of the pneumonia and pericarditis. Autopsy. Case Number 4157 entered October 1st, recovered from coma on October 3d, and died on October 10th of chronic myocarditis. She also had erysipelas and, as accessories, an exophthalmic goiter and pulmonary tuberculosis. No autopsy. Case Number 4289 entered December 7, 1924 with coma and extreme hyperthyroidism, the CO_2 rose from 11 to 25 volumes per cent. within seven hours, but she died twenty-one days later as a result of septicemia with multiple abscesses in lungs, pleura, right kidney, and a paranephric abscess, all of which may have had their origin in an abscess of the labia. Autopsy. Case Number 5176 had coma and a thyroid storm on April 13, 1926, was out of coma within twelve hours, but died on April 21st as

a result of diffuse bronchopneumonia, pulmonary embolism, and infarction and bilateral thrombosis of the median veins. Autopsy. Case Number 5784 had coma on January 14, 1927, and in four hours the blood-sugar fell from 0.53 per cent. to 0.13 per cent., developed alkalosis (CO_2 80 volumes per cent.) on January 24th which disappeared within twenty-four hours, but she died on January 27th with a non-protein nitrogen of 35 mg., blood-sugar 0.29 to 0.48 per cent. and CO_2 48 to 43 volumes per cent. Autopsy, including that of the head, revealed no satisfactory cause for death, although there was acute edema and congestion with petechial hemorrhages of the brain. Case Number 6082 died thirty-one days after coma as a result of gangrene of the leg, followed by septicemia with a mediastinal abscess. Autopsy. Case Number 6194 had a carbuncle and coma on July 25, 1927 and recovered from the latter within sixteen hours. She died of septicemia, an abscess in the brain, and abscesses in the kidneys incident to the carbuncle on August 1st. Autopsy.

Of these seven deaths after recovery from coma we believe four irremediable, but it is possible that better and earlier treatment for the underlying conditions, as well as the coma, of Case Numbers 4289, 5176, and 5784 might have led to recovery. Not one of the 14 fatal cases leads us to conclude that recovery would have taken place if alkalies had been employed.

During the last six years 8 of the 76 patients who left the hospital alive have died. Case Number 3143, died of pulmonary tuberculosis after 1.7 years; Case Number 4194, of gangrene seven days after being discharged against advice; Case Number 5065 of angina pectoris in two years; two, Case Numbers 2801 and 5187, of coma in the course of infections, while Case Number 4535 succumbed either to coma or hypoglycemia three days after discharge, probably refusing a doctor's help because of chagrin that she had developed acidosis so soon.

The 70 cases who remained alive of the 90 who together had 105 attacks of coma in the hospital have now had diabetes for an average period of 5.3 years. These patients who have had coma, therefore, compare favorably so far as duration of life is concerned with the fatal cases of diabetes in the Naunyn, Allen,

and Banting Epochs in our series who withstood the disease for four and eight-tenths, six, and seven years respectively. They have in fact already lived 1.8 years upon the average since they recovered from coma.

Of the ten patients dropped from our original first and second series, two have since died of tuberculosis and one of cause as yet unknown to us.

Explanation of the Low Mortality of the Present Series of Cases of Coma.—The mortality in our first (revised) series of 24 attacks of coma in 24 patients was 5 or 21 per cent., in our second (revised) series of 28 attacks of coma in 25 patients was 14 per cent. and in this third series of 53 attacks of coma in 50 patients is 9 per cent. What is the reason for this favorable change? Why are we able to report 48 recoveries in 53 coma cases without the use of alkalies? If alkalies would not have lowered the number of deaths is the omission of alkalies the cause of their small number? We believe not, but ascribe our results to a variety of factors:

1. Fortune favored us in our recent series. We were handicapped by but two absolutely hopeless cases instead of by five as in the earlier.

2. Experience counts. If two of the first series had fallen into our recent series in our opinion they would have recovered. In other words, today our treatment is more alert and aggressive, yet still not sufficiently so as Case Number 6983 perhaps proved.

3. The coma clientele at the Deaconess Hospital is more favorable for treatment than in most hospitals, not so much because the patients are of a different social status, but because a considerable number of them, 53 per cent., are former patients. This may explain why they do not sink so deeply into coma before they seek admission. A second reason is that they are sent to the hospital by physicians who are conversant with our attitude toward coma and methods of procedure and therefore adopt unusually prompt measures to get the patient into the hospital or better still inaugurate treatment before the patient leaves home. Vigilance in diagnosis and celerity in therapeutic action mean everything in the treatment of diabetic coma and

the value of these qualities has been increasingly recognized year by year by the profession in this vicinity. At the Deaconess Hospital all have attempted to cöoperate by considering diabetic coma to be a grave emergency and to hasten admission by the avoidance of red tape.

4. The fourth explanation relates to treatment which will now be discussed.

Treatment.—Our own methods of treatment, as described in our last clinic and elsewhere, have improved and may be summarized as follows:

1. The hospital is prepared in advance for the admission of coma patients. Typewritten directions for house officers and nurses are upon the diabetic wards. When the admitting office hears of a case about to come in, the diabetic floor is immediately warned and in turn the visiting physician, the house officer, and the laboratory, and provision for adequate special nursing both temporary and permanent is made.

2. If the diagnosis is obvious at a glance, insulin, usually 20 units, upon occasion 40 or 50 units, would be injected before the patient is undressed and indeed at times has been given before removal from the ambulance. Thereafter insulin is given every thirty minutes according to the condition of the urine and blood, utilizing reports based upon specimens of urine obtained by catheter if necessary, and upon tests of the blood for CO_2 and blood-sugar. A duplicate of the subcutaneous dose is occasionally given intravenously, but it never replaces the subcutaneous injection.

3. Warmth to the patient. Blankets temporarily instead of sheets, heaters.

4. Caffein sodium benzoate 0.5 gm. ($7\frac{1}{2}$ grains) every two or three hours as necessary until, if required, five doses have been injected.

5. Cleansing enema.

6. Salt solution 1000 c.c. subcutaneously.

7. Always with children, usually with adults, the stomach is emptied by lavage, but with the utmost gentleness.

8. Hot liquids are given by mouth at a rate not exceeding a

TABLE 3

Pathology of Diabetic Coma

A—Cases Without Recovery from Coma.

Clinical.						Pathology.				
						Pancreas.				
Case No.	Sex.	Age at coma, years.	Duration of diabetes, years.	Date of death.	Insulin total units.	Size.	Islands of Langerhans.		Acinar sclerosis.	Other organs.
							Number.	Condition.		
1305	M.	16	5.5	1922	40	Small	Normal	Sclerosis +	++	Sclerosis of myocardium and of aorta.
1870	M.	15	1.6	1920	0	Small	Normal	Lymphocytes	0	Dilatation of stomach.
2446	M.	36.9	1.1	1922	100	50 gm.	Normal	Normal	0	Aortitis, lobar pneumonia.
3240	F.	15.3	0.7	1923	60	Small	Few	Normal	0	Dilatation of stomach.
3267	F.	43	2.8	1925	290	85 gm.	Few	Sclerosis +. Acute pancreatitis, fat necroses.		Cholelithiasis, coronary sclerosis, chronic nephritis, marked general arteriosclerosis.
4525	F.	54	2.1	1925	497	80 gm.	Normal	Normal	+	Abscess of labium, general peritonitis, septicemia, acute nephritis, adenoma of thyroid.
6759	F.	49	3.8	1928	260	Excessive postmortem changes				Pyelonephritis, multiple abscesses of kidneys, congestion of lungs, coronary calcification.

B—Cases Fatal After Recovery from Coma.

Clinical.						Pathology.					
						Pancreas.					
Case No.	Sex.	Age at coma.	Duration of diabetes.	Duration of life after recovery from coma, days.	Insulin during coma.	Size.	Islands of Langerhans.		Acinar sclerosis.	Other organs.	Cause of death.
							Number.	Condition.			
2988	F.	56	4.0	6	160	Normal.	Normal.	Hyaline ++.	++	Bronchopneumonia, pericarditis, chronic nephritis, coronary sclerosis.	Pericarditis.
4289	F.	29	0.1	21	145	30 gm.	Few large.	Lymphocytes.	0	Pyelonephritis with many abscesses of kidneys, labial abscess, pulmonary abscesses, exophthalmic goiter.	Septicemia.
5176	F.	43	2.7	9	305	Small.	Normal.	Normal.	+	Hyperthyroidism, pulmonary embolism and infarction, empyema, thrombosis basilic vein.	Pulmonary embolism.
5784	F.	54	0.2	13	75	Normal.	Normal.	Sclerosis.	0	Edema meninges and brain, moderate arteriosclerosis, interstitial nephritis.	Alkalosis and tetany.
6082	F.	52	5.9	31	165	45 gm.	Normal.	Hyaline +.	+	Gangrene and amputation of leg, mediastinal abscess, pneumonia, empyema vascular nephritis.	Sepsis and uremia.
6194	F.	60	1.1	5	110	85 gm.	Normal.	Hyaline +.	+	Carbuncle of neck, abscesses of pons and kidneys, central necrosis of liver, chronic vascular nephritis, arteriosclerosis.	Carbuncle and septicemia.

glassful an hour and the preference of the patient is respected as soon as he revives sufficiently to express it. Coffee, tea, water, oatmeal gruel, orange juice, ginger ale are the favorites, and in one form or another the patient is expected to receive 50 gm. of carbohydrate during the first twenty-four hours. At times it may be necessary to give this as glucose intravenously or subcutaneously, to insure absorption.

9. The real secrets of successful treatment of diabetic coma are first the recognition of the seriousness of coma and second the willingness of the visiting staff of the hospital to remain in the hospital day and night until recovery of each case is assured.

One cannot predict the exact measure to be employed an hour in advance; one must see and examine the patient and correlate the symptoms and physical signs with the reports from the laboratory. Close supervision of the efforts to cure the coma is demanded. During the first sixty minutes after entrance each minute of the time of two nurses can be utilized under the direction of a head nurse who has seen many coma cases treated. Day or night the services of a laboratory technician will furnish valuable and almost essential data. As a rule at the Deaconess Hospital the coma team consists of one visiting physician, one house officer who at night does the tests for CO_2, blood-sugar, urine-sugar, and non-protein nitrogen, and for the first hour of treatment two nurses. The treatment accomplished the first two hours is worth more than all that expended later.

To make such a fuss about the treatment of coma may seem to many a mistake. In a way treatment is simple, provided it is prompt and alert, and sufficient insulin, salt solution and cardiac stimulation are employed as well as gastric lavage. But coma is treacherous and the pitfalls are abundant such as blocked kidneys, hypoglycemia, alkalosis even without the use of alkalies, undernutrition, a dilated stomach or failing heart, and all these are quite apart from the treatment of the condition which brought on the coma. Promptness in recognizing acidosis and energy in treating it make it possible to diagnose the underlying acute infection and so to give proper treatment. When delay in diagnosis is coupled with half-hearted treatment, a state of prostration

is soon reached in which the diagnosis of complications is absolutely impossible. The treatment of coma is the equivalent of a major operation and after our experience with these 105 cases we still feel that we must stay by the patient whether it is day or night.

Pathology.—In Table 3 are summarized the autopsy findings of 13 patients dying during coma or shortly after recovery from coma. Three of the 13 cases were treated before 1923 when the present series of coma cases was begun. The pathologic findings will be taken up according to separate organs.

Pancreas.—The pancreas was noted to be small in 6 out of 13 cases, but it is always difficult to estimate the amount of pancreatic tissue when there is any considerable invasion of the gland by fat. The islands of Langerhans were described as normal in 4 of the 13 cases and in one the postmortem changes were too extensive to permit of any description. In 3 cases sclerosis of the islands was present and in three hyaline changes. As in non-coma cases, hyaline changes in the islands were found only in patients over forty-five years of age. Sclerosis of the islands was present in one case in which the duration of diabetes was but two months. Acinar sclerosis was present in 7 cases all of whom with one exception had a duration exceeding two years. In general these changes are similar to those found in the larger series of diabetic autopsies published by Warren and Root.[1] Even upon division of the cases according to their recovery or non-recovery from coma there were no differences to be seen. Coma apparently does not produce any characteristic morphologic lesions in the pancreas.

Liver.—The changes found in the liver were not striking. In two instances fatty metamorphosis was noted, but the point of chief interest was the presence of glycogen. Four of 6 cases studied for glycogen had none, whereas in 13 of 19 non-coma deaths glycogen was present in the nuclei or cells of the liver.

Kidneys.—Unexpected pathologic changes were found in the kidneys in 4 of the 13 cases. In 4 of the 13 cases acute septic processes were present and in 7 chronic vascular nephritis was present; in fact, every case over thirty years of age showed

[1] Warren and Root, Am. Jour. Path., 1925, 1, 415.

chronic vascular nephritis. In the 4 cases with septicemia there were embolic processes in the kidney or evidences of toxic effects. In one case an acute glomerular nephritis was present. There was, therefore, pathologic evidence of renal disease sufficient to account in part for the nitrogen retention so commonly found in coma. Furthermore, the presence of renal lesions of such a serious nature was seldom evident during life. Case Number 6759 for example died with profound shock and until the autopsy no hint was obtained of the multiple abscesses in the kidneys which had left but little real functioning renal tissue. The lesions of the kidneys found at autopsy did not suggest any peculiar type of nephritis produced by coma. Krause[1] reports 3 cases of diabetic coma, who were relieved by insulin, but eventually developed anuria, uremia, and death. At postmortem the kidneys were swollen, edematous, anemic, and there was fatty degeneration of the parenchyma of the epithelium of the tubules as shown by trophic and vascular degeneration.

Heart and Arteries.—Ten of the 13 cases showed arteriosclerosis in the aorta, coronary, or renal vessels. Two children, Case Numbers 1870 and 3240 who had had the disease but 1.6 and 0.7 years respectively and one adult twenty-nine years of age, Case Number 4289, who had had diabetes but one month failed to show it. Case Number 1305, age sixteen years, with diabetes of 5.5 years duration had a well-marked arteriosclerosis in the arch of the aorta. Coronary sclerosis in fact was present in every case over thirty-seven years of age irrespective of duration which varied between 1.1 and 5.9 years, and in the only case of the four under thirty-seven years who had had diabetes five years. Case Number 2446 had well-marked aortitis probably due to lues. Along with the coronary sclerosis and paralleling it in degree were signs of myocardial degeneration. In none of these cases (the patient Case Number 4157 was not in the group), could heart-failure be assigned as the cause of death.

Pathology of diabetic coma amply confirms the clinical judgment that coma is essentially an accident. It is an acute state, not necessarily a part of the course of the disease, and usually

[1] Krause: Klin. Wochr., 7, 1622, 1928.

of such short duration as not to leave morphologic changes as an evidence of its presence.

Causes of Death.—The autopsy disclosed unsuspected pathologic conditions sufficiently severe to have produced death in 6 out of the 13 cases, as follows:

Case No. 2446—Lobar pneumonia,

Case No. 2988—Pericarditis,

Case No. 3267—Acute pancreatitis,

Case No. 4525—Acute peritonitis and septicemia,

Case No. 6082—Mediastinal abscess, pneumonia, and empyema,

Case No. 6759—Pyelonephritis and multiple abscesses of kidneys. In four others anticipated lesions adequate to explain the fatalities.

In three children there was no pathology, barring arteriosclerosis in one, except dilatation of the stomach. Case Number 1870, age fifteen years, died before the discovery of insulin, Case Number 1305, age sixteen years, treated about two months after the first use of insulin, received too little insulin, and Case Number 3240, age fifteen years, died within six hours of her admission to the hospital, and also received too little insulin. Dilatation of the stomach was present in all three. In the last, in spite of enemata and attempted gastric lavage, the stomach was tremendously dilated and the small intestine was filled with feces. In fact, virtual upper intestinal obstruction was present due apparently to toxic paralysis of the intestinal musculature. One may compare advanced coma with upper intestinal obstruction and find interesting similarities. In both occur repeated vomiting, a lowering of the plasma chlorid, and an elevation of the non-protein nitrogen of the blood. In coma the plasma bicarbonate is greatly reduced because of replacement by the ketone acids, whereas alkalosis results from uncomplicated intestinal obstruction. In both conditions dehydration is the common factor and the administration of liquids replenishing the chlorid of the blood is the common therapeutic indication.

Etiology.—Ignorance and folly were responsible for diabetic coma in all save 2 of 53 admissions at the New England

Deaconess Hospital between May, 1927 and February, 1929. The folly is that of the very young, because 23 or nearly one half of the patients in this latest series were children and 40 of the total 105 consecutive coma admissions occurred in children. Coma is no respecter of age, however, because Case Number 7021, when seventy years old, recovered and so far a search of the literature has failed to reveal her equal.

Indiscretion in diet was the most common single cause, as one would expect with so large a proportion of youthful cases. This occurred in 34 instances, and is practically the same percentage as was found in the preceding series. An infection even of a relatively mild nature has long been recognized as a precipitating factor in the production of acidosis and is well illustrated in our present group. In the course of the influenza-like epidemic during January of this year 8 patients were treated in the hospital for coma, by far the largest number for any one month. All but one of these had an upper respiratory infection. Thus, in a single month, because of a prevalent infection, as many patients had coma as in any four months for the past five years.

Infections wisely treated do not often result in coma. In only 5 cases was the infection severe, although in 13 of the 53 patients it was present. Case Number 6194 had a carbuncle which ended in fatal septicemia and in Case Number 6759 pneumonia was complicated by an abscess of the kidney with fatal outcome. Of the remaining 8 cases with precipitating infections reduction of insulin during the infection and histories of irregularities of diet were important etiologic factors.

Among adult patients with the inception of pre-coma symptoms or in the presence of a gastro-intestinal upset from whatever cause, repeatedly it has happened that insulin has been omitted or reduced. This is in spite of a rule that every patient is told with such complications never to omit insulin unless the urine is sugar free, and to test the urine at such times at least four times a day.

The patient who has avoided regular medical supervision offers a fertile soil for the onset of coma. Forty-seven of the 53 patients were not under even fairly close supervision either

by their family physician or ourselves. It is good insurance for a diabetic patient to report to his doctor once a month. With the children of the Joslin Diabetic Unit we are trying in some unobjectionable way to bring this about.

Although coma did occur in 34 of the patients who had been treated by us on previous occasions, 26 of this number were children. But the children deserve a good deal of credit for there were but 5 of them who had had more than one admission for coma at the New England Deaconess Hospital.

Of the entire 105 cases but 10 have been repeated offenders. Of the two patients, Case Numbers 2786 and 3391, the former reduced her insulin in the presence of infection and the latter had infection on the second admission. The first coma was caused by broken diet in both instances. Case Numbers 4535 and 3129 were diet offenders both times. Of the younger diabetics all entrances, save the third admission, Case Number 4232, were due to broken diet. Case Number 3877 has the greatest number of comas to her discredit, 5 attacks in 2.5 years, but she has had none for the last 1.4 years. Case Number 6287 has had coma three times in the present series. On routine intelligence test her intelligence quotient was found to be only 80, and her home environment is the poorest of any patient in the entire series of more than 350 living diabetic children.

These ten patients had coma 25 times. One of the number is dead, one has probable pulmonary tuberculosis and cataracts, two are below height and weight, 6 are in good condition.

TABLE 4

PRESENT STATUS OF REPEATED COMA OFFENDERS

Case No.	
2786, 3391	Coma January, 1929. Both recovered.
3040, 3877	Physical condition good. Diabetes decompensated.
3682, 6287	Below height and weight. Decompensated.
3129, 6767	Physical condition good. Sugar free most of the time.
4232	Tuberculosis and cataracts. Sugar free most of the time.
4535	Dead.

Insulin was given for the first time to 16 of the patients after they developed coma. This is similar to the series of deaths from diabetes reported by the Metropolitan Life Insurance

Company in 1925. Less than half of the patients received insulin among the 1800 total cases and not less than 17 per cent. of these until within one day of death. Indeed the diagnosis of diabetes was not made in 3 of the cases, Case Numbers 6759, 7152, and 7557, until they had contracted coma, and of these the first two died.

Coma can break out in controlled diabetes at short notice. Case Number 1616 fell on the ice during an insulin reaction and had a slight concussion. Nausea and vomiting unfortunately led to the omission of insulin and coma developed in sixteen hours after recovery from hypoglycemia.

Clinical Features.—*Duration of Diabetes at Onset of Coma.*—The duration at the time of onset of coma has increased with each coma series. In the first series it was 2.4 years, in the second 2.8 years, and in the third 4.0 years. This is coincident with the increase in duration of life particularly of the increase in duration of life of the children. These durations may be compared with similar figures compiled for 122 fatal cases of coma occurring almost exclusively outside of the hospital in 1926. In that group the duration was 5.3 years. The average duration of diabetes in the present series is 3.2 years.

Symptoms and Signs of Coma.—Nausea, vomiting, restlessness, drowsiness, hyperpnea, dehydration, coma, hyperglycemia, ketonemia, glycosuria, ketonuria are the cardinal symptoms and signs of diabetic coma.

Circulation.—Circulatory and renal failure though not the rule are important. Circulatory failure as evidenced by a blood-pressure below 90 occurred in but 5 adult patients. Two adults had blood-pressures of 70. Case Number 6729 with blood-pressure of 60 recovered, but Case Number 6759 whose blood-pressure was 30, although it rose temporarily with adrenalin and ephedrin to 90, and Case Number 7152 whose blood-pressure was 60 each had a fatal outcome.

Tachycardia with regularity of the pulse has been the rule in our patients, but a young patient, Case Number 7486, did have extra systoles. Auricular fibrillation as a consequence of diabetic acidosis is reported by Borg.[1] In a victim of repeated

[1] Borg: Jour. Amer. Med. Assoc., 1928, 91, 1064.

TABLE 5

DURATION OF DIABETES PRECEDING COMA IN A SERIES OF 122 PATIENTS COMPILED IN 1926 COMPARED WITH THE DURATION OF DIABETES IN 105 CONSECUTIVE CASES OF COMA TREATED AT THE NEW ENGLAND DEACONESS HOSPITAL

Duration of diabetes to death from coma from 1922 to 1926.			Duration of diabetes at the time of onset of coma in 105 consecutive coma admissions at the New England Deaconess Hospital.		
			Series I 1923–1925	Series II 1925–1927	Series III 1927–1929
0– 1	8		8	8	8
1– 2	20		6	2	9
2– 3	24		4	9	5
3– 4	16		1	4	6
4– 5	7		3	1	4
5– 6	6			3	5
6– 7	3				9
7– 8	10				3
8– 9	8				3
9–10	3		2		
10–11	5				
11–12	1				
12–13	2				
13–14	2				
14–15	2				1
15–16	1				
16–17	0				
17–18	1				
18–19	0			1	
19–20	2				
20–21	1				
	Average = 5.3 yrs.			Average = 3.2 yrs.	

attacks of acidosis auricular fibrillation was observed during two attacks. This was relieved when the patient's general con-

dition improved with insulin. In 2 of our own fatal cases, Case Numbers 7152 and 6759, the picture of profound circulatory collapse existed for sixteen and six hours respectively in spite of the administration of fluids and cardiac tonics.

Cardiovascular collapse in diabetic coma is reported by Labbé and Boulin.[1] They describe three such cases as a type observed since the use of insulin in treatment of coma. According to them there is a typical onset with rapid pulse, low blood-pressure, sugar, and acid. Improvement follows treatment, but tachycardia and hypotonia persist and increase. The extremities remain cold and the patient dies in spite of treatment with cardiac tonics. They believe this due to hypotension resulting from a toxic inhibition of the bulbar vasomotor centers.

In our series Case Number 6759 at autopsy did not show pathologic evidence of damage to the circulatory system, but proved to have pneumonia and kidney abscess.

Determination of the minute volume of the blood in 3 cases of diabetic coma by Lauter and H. Baumann[2] is confirmatory of the circulatory signs. A fall in volume with onset of coma took place and this continued in spite of the use of insulin. It was not observed in cases of grave acidosis unaccompanied by signs of coma. In like manner well-marked diminution in circulatory blood volume in diabetic acidosis was found by Chang[3] et al., in five patients.

Renal Function.—Casts and albumin are the rule. Anuria occurred in Case Number 7157 of the present series for eleven hours preceding death. The highest non-protein nitrogen, 140 mg. per 100 c.c., occurred in Case Number 6052 and was associated with extreme hyperglycemia. Hyperglycemia and nitrogen retention are largely associated with one another. No patient with a non-protein nitrogen over 80 mg. per 100 c.c. had a blood-sugar below 0.57 per cent. Diacetic acid was absent only in Case Number 6082. At autopsy examination of the kidneys showed multiple abscesses.

[1] Labbé, Boulin, Paris Med., 1928, 36, 257.

[2] Lauter and Baumann: Jour. Amer. Med. Assoc., 1928, 90, 4, 1985.

[3] Chang: Deutches Archiv. für Klinische Medicin, Leipzig. (Landsberg: Deutsch, Med. Wchnschr., 1928, 54, 2100.)

The non-protein nitrogen of 7 of 53 patients was 80 mg. per 100 c.c. blood or over at the time of entrance to the hospital. Three of these had a fatal outcome, although the patient with the highest value, 140 mg., recovered. Of the 6 fatal cases in this series one half had a non-protein nitrogen of 80 or over. The ages of these patients varied from 14.0 to 51.2 years and the duration of diabetes from 0.7 to 6.4 years. Kidney pathology was demonstrable by autopsy in 2 of the fatal cases, Case Numbers 6194 and 6759. There were multiple abscesses in both instances. Non-protein nitrogen estimations were not done routinely on all patients on the second day. In the 24 estimations made there was no evidence of rise after initial treatment.

Van Paassen[1] studied disturbances of kidney function shown by urea retention, decreased excretion of ammonia and phenolphthalein, and blockade phenomena such as an altered relation between ketonemia and ketonuria. There was no constant difference in these respects between cases with recovery and those without. During treatment disturbances of water secretion were produced by the large doses of insulin. Dehydration was the rule and in addition to this element, which the body would tend to compensate for, was the element of storage of glycogen which would follow the use of insulin.

TABLE 6

COMA CASES WITH HIGH NON-PROTEIN NITROGEN.
(80 MG. PER 100 C.C. OR MORE)

Case No.	Age at coma, years.	Duration D.M.	Sugar.	Blood CO_2	N.-P.N.	Urine.		Insulin.	Result.
						Diacetic acid.	Sugar.		
4099	20.0	4.0	1.62	13	140	plus	1.6	255	Recovery
4250	14.0	4.9	0.92	8	98	2 plus	2.0	210	Recovery
5033	22.0	0.7	0.86	6	80	4 plus	3.9	440	Recovery
6082	51.2	6.4	0.57	13	154	0	trace	60	Fatal
6759	48.9	3.8	0.70	9	82	2 plus	3.0	260	Fatal
6983	30.8	0.8	1.04	10	80	4 plus	5.0	400	Fatal

Hyperglycemia over 1 per cent. occurred three times with recovery twice. Case Number 4099 has the highest blood-sugar (1.62 per cent.) with recovery we have found in the literature.

[1] Van Paassen, Jour. Amer. Med. Assoc., 1928, 91, 19.35

The case is reported in detail by Curtis and Dixson.[1] The chemical changes in the blood are shown in Table 7.

TABLE 7

CHEMICAL CHANGES IN BLOOD IN A PATIENT WITH EXTREME HYPERGLYCEMIA

Time.	Blood-sugar, per cent.	Non-protein nitrogen. mg. per 100 c.c.	Blood carbon dioxid, per cent. by volume.
6 A. M.	1.62	140	13
8 A. M.	1.38	103	18
11 A. M.	0.79	80	24
3 P. M.	0.36	80	37
6 P. M.	0.13	78	48

On admission the patient exhibited all the symptoms and signs of extreme acidosis: soft eyeballs; Kussmaul respiration; acetone odor of the breath; a rectal temperature of 96.6° F.; urine containing three plus sugar and diacetic acid; a blood-pressure of 95 systolic and 75 diastolic; a pulse rate of 140; a white-blood count of 28,100; blood carbon dioxid, 13 per cent. by volume; blood-sugar, 1.62 per cent. (checked twice), and non-protein nitrogen, 140 mg. per 100 c.c. During the first eight hours she received 225 units of insulin subcutaneously—20 units every thirty minutes for ten doses, then smaller doses hourly. Specimens of urine were obtained by catheter every two hours. We thought it inadvisable to attempt to lower the blood-sugar at too rapid a rate because of a possible ill effect on the heart. The accompanying table shows the chemical changes that took place in the blood from time to time.

Comparatively little insulin was administered after 10:30 on the morning of admission, and yet as can be seen from the table the blood-sugar continued to drop rapidly. The specimens of urine continued to show sugar, although in decreasing amounts.

Neither dextrose nor any carbohydrate drinks were given for the first eight hours. Then 100 gm. of carbohydrate was ordered for the next twenty-four hours to be given as orange juice, ginger ale, or any other drink that the patient would tolerate. Her condition rapidly improved, although it was twenty-four hours before complete consciousness was restored.

[1] Curtis and Dixson: Jour. Amer. Med. Assoc., 1928, 90, 1115.

She was discharged October 10, 1927 on a diet of 80 gm. of carbohydrate, 55 gm. of protein, and 110 gm. of fat, a total of 1530 calories, with insulin twice daily, 20 units before breakfast, and 10 units before supper.

The lowest blood-sugar in coma was 0.19 per cent. in Case Number 7565. The coma was associated with her thirteenth pregnancy. Her previous twelve pregnancies had resulted in dead babies. Naturally she excited much interest, because if the thirteenth child can be saved we shall have reason again to consider diabetes a good disease. Following recovery the patient had clinical signs of a living fetus and is now again at the hospital awaiting cæsarean section.

Weight.—Of the fatal cases one third were overweight at the time of coma. Unfortunately a weight was not always obtained. McLeod's fat dogs developed acidosis more quickly and succumbed more readily than did the thin diabetic dogs.

A CO_2 combining power below 10 occurred thirteen times. This did not indicate the use of greater amounts of insulin or delay in recovery.

Actual unrousable coma is met with less and less frequently. Both physicians and patients recognize symptoms of impending coma and send patients to the hospital early. No evidence of paralysis was found.

The loss of tolerance for carbohydrate is not the rule among these patients. The patient who has had coma is more susceptible to tuberculosis than the average. Three of the 90 patients in the entire group reported have positive tuberculosis and 4 cases have suspicious lesions.

Differential Diagnosis.—The differential diagnosis of coma was discussed in the preceding report. More recently occasions have arisen for a differential diagnosis between coma and acute surgical conditions of the abdomen. Thus in 32 patients of this series the white blood counts, with the exception of Case Number 5042, varied between 14,750 and 54,560. Four of these cases had abdominal pain, but in no instance was a surgical abdomen demonstrated. Yet within a period of a few weeks in the spring of 1928 there entered the Deaconess Hospital six diabetic patients

with appendicitis, all of whom showed acidosis, but not actual coma. The problem of distinguishing between acidosis and appendicitis, especially in children, has been described by two authors recently. Smith[1] reported four instances of acidosis in children with leukocytosis. In one, after several attacks of abdominal pain, acidosis and leukocytosis as high as 27,800, subacute appendicitis was demonstrated at operation as well as an enlargement of the liver due to hepatitis. Nevertheless later leukocytosis again characterized acidosis without inflammatory lesion. Leukocytosis may be due solely to acidosis, but the possibility of infection must be remembered, "antiketosis must rank with asepsis in the surgical conscience" (Smith).

Hamburger[2] reports a child of eight years who was about to be operated upon because of abdominal pain and was noted to have deep breathing. Glycosuria was found, and death in coma followed the next day.

Coma and appendicitis are closely related in the life of the diabetic. Each resembles the other in its early symptoms; coma is often consequent upon appendicitis either before or after operation; each has an inevitably fatal prognosis if improperly treated. The seriousness of this combination and the fact that surgeons and physicians alike must encounter it more and more frequently justifies discussion of the pitiful case of a child operated upon for appendicitis with subsequent death in coma. The description follows:

Case Number 1779 developed diabetes at the age of 3.6 years in February, 1920. Her grandfather had diabetes. When first seen on March 12, 1920 the urine contained 2.4 per cent. sugar, her weight was 16 kilograms dressed and her height was 99 cm. In 1922 she had scarlet fever. Under careful observation she did fairly well, although not always sugar free, and entered the Deaconess Hospital, April 6, 1923 for insulin treatment. At this time her urine contained 2 per cent. sugar but no diacetic acid. Her weight at this time was 19.5 kilograms and her height 112 cm. She did very well from that time on and in

[1] Smith: Jour. Amer. Med. Assoc., 1929, 92, 308.
[2] Hamburger: Münch. Med. Woch., 1928, 75, 1325.

June, 1928 a letter from her parents stated that she weighed 38 kilograms and that her height was 166.5 cm. She was taking 24 units of insulin a day and was sugar free part but not all of the time.

In the fall of 1928 she was living in a neighboring state and doing extremely well in her studies at school. Her average was 98 per cent. in all her subjects. She had won the spelling contest and the athletic championship for girls under twelve years. She last saw us in April, 1923 and it was only some weeks after her last illness that we received the following information.

It appears that on Sunday, November 25th, the child ate little supper, but had no pain or nausea. On Monday her stomach "felt bad" and calomel was given without resulting movement of the bowels. At 2.30 A. M. on Tuesday she was much worse, with "distention of the abdomen, more pain high up under the ribs, rapid pulse, distressed for breath and somewhat stupid." Repeated enemata without avail. Another physician called in consultation said "digestive disturbance." The white-blood count was 20,000 and a surgical consultant advised immediate operation for a ruptured appendix. At this time the temperature was subnormal and the abdomen distended. The hypodermoclysis apparatus being out of order she was given orange juice by mouth. At operation under gas oxygen anesthesia, a mildly inflamed appendix and neighboring bowel were found. She spoke after the operation, but the abdomen remained distended, enemata were unsuccessful and there was regurgitation of bile-stained fluid.

The urine showed albumin 2 per cent. and many granular casts. At 4.00 P. M. the blood-sugar was 0.30 per cent. and the urine contained sugar and diacetic acid. At 8.00 P. M. the blood-sugar was 0.22 per cent. and the urine contained more diacetic acid. In four hours only 1 ounce of urine was obtained by catheter. Coma, with struggling for breath, increased and she died at 9.00 P. M. Tuesday, November 27th.

Without discussing in detail the differential diagnosis we may summarize the chief lessons afforded by this case:

1. Loss of appetite with pain in the abdomen and constipa-

tion in a diabetic always suggest the onset of coma and demand instant inauguration of appropriate measures for diagnosis and treatment.

2. Distention and pain high in the abdomen indicate the need for gastric lavage. Unless performed early death may result from dilatation of the stomach even though coma is adequately treated with insulin.

3. Leukocytosis of 12,000 to 80,000 is the rule in coma and, therefore, is no aid in the diagnosis of appendicitis when coma is present. The diagnosis of appendicitis in a patient "almost comatose" is nearly impossible without a typical history of a palpable mass.

4. Albuminuria and granular casts are typical of diabetic coma, are not necessarily indicative of Bright's disease, and are rare in appendicitis. In general, the greater the dehydration in coma, the more marked will be the oliguria and albuminuria.

5. The oliguria and albuminuria must be combated with liberal amounts of normal salt solution given subpectorally or intravenously as early as the diagnosis of acidosis is made. If dehydration is allowed to proceed, anuria, uremia, and death follow.

6. Diabetic coma should never cause a death after operation.

Such a tragic ending to the life of this child reminds us that every surgical diabetic is a candidate for coma and that coma brings complicating symptoms for interpretation as well as urgent therapeutic problems. No matter how slight the operation, this dictum holds true, and only those surgeons will escape the experience of entering the ward on the day after an operation and unexpectedly finding their patients drowsy and with air hunger who take steps to prevent this complication in all cases. Urinary tests must be made at least every four hours before and after operation upon a diabetic, and insulin administered accordingly.

When in these instances emergency operations must be performed without one or two days of preparation the following diabetic routine has been found useful:

Preoperative Treatment.—(1) The size of the insulin dose is determined somewhat by the preceding insulin treatment and also by the result of the preoperative urinary analysis. (2) Twenty-five gm. of carbohydrate, as orange juice, oatmeal gruel, or bread by mouth, or a 10 per cent. glucose solution intravenously are given from one to four hours before operation.

Postoperative Treatment.—(*a*) The urine is tested upon a two-, four-, or six-hour schedule. The greater the glycosuria, the more frequently must the specimens be tested. From 5 to 20 units are given as indicated by qualitative tests. (*b*) The diet of the average diabetic recovering from an operation or coma should contain during the first two or three days 75 to 100 gm. of carbohydrate. (*c*) When acidosis complicates surgery not only food and insulin are necessary, but one must forestall dehydration, oliguria, dilatation of the stomach and circulatory collapse, and the regular regimen of coma treatment followed, such as: (1) Gastric lavage, performed whether vomiting has occurred or not and repeated if the vomiting recurs after the first lavage. (2) Normal salt solution given subpectorally, 700 to 1000 c.c. If not quickly absorbed, the intravenous injection of glucose solution will hasten absorption (Gamble). (3) Ephedrin 1 c.c. or adrenalin 1 c.c. (1 : 1000) subcutaneously when the blood-pressure is below 100 mm. systolic. (4) Repeated enemata of salt solution. (5) Caffein sodium benzoate, gr. $7\frac{1}{2}$, subcutaneously every four hours.

Prognosis.—The prognosis of coma depends upon the coexisting complications and whether the patient is first seen in an actually moribund state.

Blood chemistry is no criterion. There have been recoveries with a blood-sugar as high as 1.60 per cent., a non-protein nitrogen value of 140 mg. per 100 c.c., and a CO_2 combining power of 5 volumes per cent. A leukocyte count of 80,000 occurred during the coma of one of the children who recovered.

Pulse rates from 150 to 200 occur often among the younger patients without fatalities. One patient with a systolic blood-pressure of 60 responded promptly to treatment and is now in

good condition. Temperatures as low as 94° and as high as 103° F. have been associated with recoveries.

No systematic attention has been directed to the tension of the eyeballs, although we usually record it. More careful studies are to be carried out in the future with the help of Dr. J. Herbert Waite, who will make an investigation of the eyes of our patients with diabetes during the next three years.

The younger the diabetic, the better the prognosis. However, extreme age does not insure a grave prognosis.

In September, 1926 an elderly lady of sixty-eight years, Case Number 7021, weighing 210 pounds, and whose past history has been remarkably free of sickness, became rapidly prostrated over a period of ten days by progressive weakness, extreme thirst, and rapid loss of weight. November 10, 1926 she entered the Franklin County Hospital, Greenfield, Mass., in a nearly comatose condition and a large amount of sugar was found in the blood and urine. She was discharged on a diet of approximately carbohydrate 25 gm., protein 52 gm., fat 92 gm., with insulin 30 units. After a short time she found she was having reactions at night, and, accordingly, omitted the evening insulin. Since that time she has adhered strictly to this diet and taken insulin 20 units regularly, and done very well.

For several days before the present admission she had been feeling very tired and weak, and had been overworking and had broken her diet. She planned to see a doctor, but on the afternoon of June 22, 1928 she became rapidly worse and lost consciousness between 4 and 5 P. M. Dr. S. F. McKeen was called to see her and administered 40 units of insulin, the juice of an orange, and brought her to the Deaconess Hospital two hours after the onset of coma.

The symptoms on admission were profound coma, Kussmaul respiration, rectal temperature 97.5° F., acetone odor of breath, soft eyeballs, cold and cyanotic hands and feet, blood-pressure 120/60, pulse 104, urine 3.3 per cent. sugar, diacetic acid three plus, many hyaline and granular casts, blood CO_2 6 volumes per cent., blood-sugar 0.74 per cent., non-protein nitrogen 62 mg. per 100 c.c., white blood-corpuscles 17,500.

TABLE 8

DIABETIC COMA IN A WOMAN OF SEVENTY YEARS

Time.		Insulin.	Other treatment.	B.-S.	N. P. N.	CO_2.
Before entrance:		40				
Admitted	P.M. 6.15	50	Caf. sod. benz., gr. $7\frac{1}{2}$.			
	6.20		Catheter specimen.	0.74	62	6
	6.30	50	Gastric lavage.			
	6.35		Enema.			
	6.45		Subpect.- 1500 c.c. saline.			
	7.15			0.72		6
Responsive	8.00		Orange juice 125 c.c.			
	8.20	40				
	8.45		Water 120 c.c. hourly.	0.64	62	10
	9.10	40				
	10.00			0.54	60	10
	10.15		Caf. sod. benz. gr. $7\frac{1}{2}$.			
	10.20	15	Ginger ale 120 c.c.			
	11.05	25				
	A.M. 12.25			0.38		
	1.25	20				
Vomiting	1.30		Gastric lavage.			
	2.00		Caf. sod. benz. gr. $7\frac{1}{2}$.			
	3.30	15				
	5.30	15				
	7.30			0.11		

Her condition rapidly improved and she was discharged on the twelfth day sugar free, taking 84 gm. of carbohydrate and 65 units of insulin. Her recent reports are satisfactory.

Her course is shown in Table 8, page 39.

Condition Upon Discharge with Diets and Insulin Recommended.—Maintenance diets at discharge requiring from one and a half to twice as much insulin as the average hospital case were prescribed in nearly all instances. There were but five patients who received less than 30 calories per kilogram body weight. The least amount of carbohydrate given was 54 gm. and the greatest 169 gm. Carbohydrate over 75 gm. was prescribed in 70 per cent. of this series. The protein varied from 0.75 to 3.0 gm. per average kilogram body weight, largely according to age. The least amount of daily insulin at discharge was 20 units and the greatest was 60 units.

The average hospitalization of the patients was twelve days. One patient was discharged on the third day following recovery. One patient remained in the hospital fifty-one days because of an acute mastoiditis and pyelitis.

The recital of these cases impresses us more than ever with the appalling needlessness of diabetic coma and for its prevention we shall redouble our energies.

TABLE 9

CONDITION OF 45 PATIENTS FOLLOWING DIABETIC COMA. DIET, INSULIN, AND WEIGHT AT DISCHARGE

Years.	No. of cases.	Age at discharge.	Duration of D.M.	Diet in grams.				Wgt., kg.	Cal.. kg.	Insulin units at discharge.	Days in hospital.
				Carb.	Prot.	Fat.	Calories.				
6–10	4	7.3	1.7	85	58	92	1400	20	70	32	9
10–15	11	13.1	0.5	79	62	104	1500	32	47	39	8
15–20	5	16.6	5.6	81	68	118	1658	44	34	47	9
20–30	7	24.2	2.9	86	67	120	1692	51	33	38	14
30–40	5	34.6	5.9	100	62	111	1647	61	27	37	11
40–50	7	44.8	4.0	97	69	119	1735	54	32	37	13
50–60	4	51.4	5.0	98	64	107	1611	50	34	25	25
60–70	1	64.1	8.0	100	67	114	1694	42	40	35	18
70–80	1	70.0	1.8	84	50	100	1456	66	22	65	12

CLINIC OF DR. JOHN LOVETT MORSE

PROFESSOR OF PEDIATRICS, EMERITUS, HARVARD MEDICAL SCHOOL

SOME OF THE CAUSES OF DIFFICULT, NOISY, AND RAPID RESPIRATION IN INFANCY AND EARLY CHILDHOOD

THE usual causes of temporarily difficult or rapid respiration in infancy and early childhood are nasopharyngitis, bronchitis, bronchopneumonia, and lobar pneumonia.

Adenoids are probably the most common cause of continuous difficulty with respiration during infancy and the first few years of childhood. The degree of disturbance which they cause varies from time to time, however, according to whether there is an acute infection of the adenoids or not. The picture is characteristic, but is often overlooked. Nasal respiration is impaired and often noisy, the mouth is open, the baby snuffles more or less day and night, and snores at night. The cry is clear or nasal. The lungs are normal, although transmitted râles are often heard. In severe cases there may be at times slight retraction of the supraclavicular and lower intercostal spaces and of the diaphragm. If there is an accompanying rickets, deformities of the chest may also develop as the result of the interference with the entrance of air into the lungs. Not infrequently there is, in addition, difficulty in nursing and considerable disturbance of nutrition. It must never be forgotten that adenoids may be large enough at birth to cause symptoms.

In spite of the frequency with which adenoids cause disturbances of respiration in infancy and the characteristic picture which they show, they are often overlooked and the symptoms attributed to some other condition, the fashionable one at present

being hypertrophy of the thymus. The following cases are examples of this mistake:

A baby, three and one-half months old, had had trouble with breathing from birth. It had had four treatments with the Roentgen ray, the first when it was three weeks old. There had been a little improvement in the symptoms. The physician in charge wished the baby to have further treatments, but the roentgenologist was unwilling, although the thymic shadow was but little smaller than in the beginning. The baby was constantly snuffling and had much difficulty in breathing with its mouth shut. It made a little noise in inspiration. None of the characteristic signs of enlargement of the thymus were present. A large amount of adenoids was felt with the finger. They were removed the next morning. That night the baby slept quietly. There has been no return of the symptoms after fifteen months.

A baby, seen when nine months old, had snuffles and breathed peculiarly at birth. A roentgenogram taken at three months showed what was supposed to be an enlarged thymus. It was treated with radium and had had half a dozen roentgenograms taken, each of which, of course, amounted to a treatment. The symptoms had increased, nevertheless, up to a month before, since when they had remained unchanged. The baby was constantly snuffling and snorting, could not breathe with its mouth shut, had difficulty in taking its bottle and showed none of the classical symptoms of enlargement of the thymus. A large amount of adenoids was felt with the finger. The adenoids were removed, in spite of the supposed enlargement of the thymus, without difficulty and with immediate improvement.

In other instances the symptoms of adenoids are not as characteristic and may lead to much confusion principally because of the reflex symptoms and secondary congestion which they may cause. The following history is an example:

This baby began to sneeze and cough a great deal at two weeks. There was continuous slight wheezing. After six weeks a roentgenogram of the thymus was taken which showed it to be normal. At six months a bronchoscopy was done and the larynx and bronchial tubes found to be inflamed. After that it had repeated treatments with the ultraviolet lamp and had all its food stopped except milk boiled for an hour and orange juice. During all this time it had repeated colds. Whenever it had a cold, the wheezing and coughing were worse. It was seen when ten months old. It was well developed and nourished and of good color. There was slight retraction of the lower ribs with inspiration. There was a wheezing noise with expiration. Although it kept its mouth shut, the whole upper pharynx was blocked by a very large amount of adenoid tissue. The whole throat was full of mucus, reddened, and edematous. The tonsils were much enlarged. There was a

frequent wheezy cough. The voice was clear. Air entered both lungs alike. Nothing abnormal was detected in the lungs, but expiration was prolonged. New roentgenograms showed no enlargement of the thymus and clear lung fields. The difficulty in breathing was evidently due to reflex irritation in the larynx from congestion in the adenoids and nasopharynx. The parents, however, refused to have the adenoids removed.

Hypertrophy of the Thymus.—As already hinted, the tendency of physicians at present is to attribute all disturbances of respiration in infancy to hypertrophy of the thymus. In the vast majority of the cases which I have seen, in which the symptoms have been attributed to enlargement of the thymus, they have manifestly been due to other easily discoverable causes, in spite of the fact that roentgenograms were supposed to show an enlargement of the thymic shadow. There is no doubt that hypertrophy of the thymus does occur and that the pressure of the enlarged thymus on the structures behind it may cause disturbance of the respiration. These symptoms may be either continuous or intermittent, as the size of the thymus varies according to how much blood it contains. The pressure is exerted chiefly on the trachea, although the veins may at times be slightly compressed. Pressure on the trachea causes noisy respiration, dyspnea, retraction of the intercostal spaces, and cyanosis. If the pressure is sufficient to cause noisy respiration, it will be noisy in both inspiration and expiration, because the pressure on the trachea is exerted during both inspiration and expiration. It is evident, therefore, that when inspiration only is noisy, the cause is not enlargement of the thymus. When noisy respiration is due to the pressure of an enlarged thymus, it is increased by extension of the head, which narrows the upper opening of the thorax. When the thymus is enlarged enough to cause symptoms of pressure, it is almost always palpable in the suprasternal notch and there is definite dulness under the manubrium. Furthermore, the larynx is not depressed during inspiration because it is kept up by the enlarged thymus. When the thymus is enlarged enough to cause symptoms and physical signs, the Roentgen ray will, of course, show a large thymic shadow. A large thymic shadow, in the absence of the characteristic symptoms and physical signs of enlargement of

the thymus, does not prove, however, that other symptoms, often erroneously attributed to enlargement of the thymus, are due to it. In fact, it should never be necessary to take a roentgenogram of the thymus to determine whether or not certain symptoms are due to the pressure of an enlarged thymus. Likewise, it should not be necessary to take roentgenograms to determine that certain symptoms are not due to an enlarged thymus. It should be plain that they are not due to it, even if the shadow is enlarged, without taking into consideration all the errors which are associated with roentgenograms of the thymus.

A characteristic example of the symptomatology of hypertrophy of the thymus is the following:

It was noticed when this baby was six months old that her respiration was unusually rapid and that at times it was a little difficult. The mother was not sure, however, that these symptoms had not been present previously. The symptoms gradually increased during the next two months. The respiration continued rapid and was often a little wheezy, the wheeziness occurring both with inspiration and expiration. She was at times a little blue, but never markedly so. She never appeared uncomfortable, however, and apparently was not inconvenienced in any way. Slight suprasternal retraction developed at about eleven months and dulness was found under the manubrium. She was seen when one year old.

She was well developed and nourished and of good color. She was bright and happy and seemed perfectly comfortable. She kept her mouth shut and there was no nasal discharge. Her throat was normal to inspection and palpation. Her voice and cry were clear. The respiration was rapid but regular. There was slight suprasternal retraction with inspiration. The relation between inspiration and expiration was normal. When she was quiet, the respiration was inaudible. When she was active or excited, it became a little wheezy. The wheezing was usually more marked in expiration than in inspiration. Extension of the head increased the wheeziness. An indefinite resistance was felt in the suprasternal notch, this resistance being more marked during expiration than during inspiration. There was moderate dulness under the upper portion of the manubrium. The heart and lungs were normal. The intensity of the respiratory sound was the same on both sides. There was no dulness in the interscapular region and the respiratory and voice sounds were normal in character over the upper dorsal spines.

Congenital Laryngeal Stridor.—Another cause of noisy although not of difficult or rapid respiration in infancy, which is present from birth on, is congenital laryngeal stridor. In this condition, which is caused by a congenital narrowing or infolding

of the epiglottis with consequent laxness of the aryepiglottidean folds or to a congenital elongation of these folds, a crowing sound is made with inspiration. It is never heard in expiration. It is constant, but varies in intensity with the depth of the respiration. There are no other symptoms and no physical signs except the deformity of the larynx. The baby is perfectly well, except that it makes a noise in inspiration—"child crowing." Examples of this condition are the following:

The nurse noticed in the first week that this baby made a peculiar noise in breathing. This noise continued and became a little more marked. It was scarcely noticeable when the baby was perfectly quiet, but increased a great deal when it was crying or excited. The baby was apparently not in any way disturbed or discommoded by the noise and never became cyanotic. It was seen when four months old.

It was a nice, large, fat, healthy looking baby, bright and happy. It made a bubbling, crowing noise with inspiration. This noise was more marked at some times than at others. It was not very long or high pitched. It increased when the baby cried. The color did not change even when the noise was loudest. There was no nasal obstruction. The fauces were normal. The thymus could not be felt. There was no dulness under the manubrium. There was no retraction. The lungs were normal and air entered both sides alike. There were no evidences of enlargement of the tracheobronchial lymph-nodes.

Noisy breathing was noticed in baby B. also during the first week. It became much louder during the next three weeks, since when it had increased a little. The noise was always audible, whether the baby was asleep or awake. The night before it was seen the respiration could be heard through two doors and a hall. She was seen when two months old.

She was fairly developed and nourished and of good color. She had slight snuffles and there was a tendency to keep the mouth open. The throat was normal to inspection and palpation. She made a crowing noise with each inspiration. When excited it was loud and hoarse. Tipping back the head did not increase the noise. There was no dulness under the manubrium. The thymus was not palpable. The lungs were normal. The air entered both sides alike. There was no evidence of enlargement of the tracheobronchial lymph-nodes.

Roentgenograms showed no enlargement of the thymus and nothing abnormal in the lungs. A throat specialist, however, found a large, loose epiglottis.

Atelectasis of the Lungs.—The most common causes of disturbances of respiration in the first few days of life are cerebral hemorrhage and atelectasis of the lungs. The symptoms of

atelectasis of the lungs are usually evident at once, but not infrequently they may not be noticed for several hours or even days. In very feeble and premature babies they may be so obscured by the general feebleness and cyanosis that they are overlooked entirely. I have repeatedly seen atelectasis of the lungs at the autopsies of premature babies, who had lived for several weeks, in whom the condition had never been suspected and had not been discovered on physical examination. The symptoms, which are chiefly rapid respiration and cyanosis, may be continuous or intermittent, slight or marked. They are, of course, increased by exertion, such as crying or nursing. The cry is usually feeble. Incidentally, the fact that a baby cried at birth does not rule out atelectasis of the lungs. The physical signs are often very indefinite, because of the small size of the lungs and the transmission of sounds from one side of the chest to the other. Inspection seldom shows any diminution in the respiration on the affected side. Percussion is unreliable, because the lungs are so small, the chest is so elastic, and the compensatory emphysematous areas obscure the dulness which would be expected from the atelectatic areas. The respiration is usually superficial and the normal sound in the expanded areas prevents the bronchial sound from the unexpanded areas, into which little air enters, from being noticed. While theoretically there should be bronchial respiration over the atelectatic areas, practically the sound which is heard is vesicular or, at most, bronchovesicular. The voice sounds should be bronchial over the atelectatic areas, but the baby seldom cries loudly, the sounds are mixed with those from the expanded emphysematous areas and, in consequence, they are, at most, only bronchovesicular. Moist râles are sometimes heard over the atelectatic areas.

The Roentgen ray, however, gives most valuable information as to the presence or absence of atelectasis and as to whether the lungs expand or not as time goes on. The atelectatic areas, of course, show a shadow.

The following cases are examples of different types of this condition:

Baby L. was twenty-four hours old when it was seen. The labor was very rapid. No anesthetic was used. The cord was around the baby's neck when it was born, but apparently had done no harm. It cried fairly loudly soon after birth, but had cried but little since then. It was slightly cyanotic at birth. It was more so in half an hour and in five hours was so cyanotic that artificial respiration was done and oxygen given. Since then it had improved. It was noticeable that the cyanosis was less when it cried than when it did not.

The baby appeared normal except for moderate cyanosis. The respiration was normal in rate and character. The heart was normal. There was no dulness under the manubrium. The thymus was not palpable. There was slight dulness in the right axilla, but nothing abnormal could be detected about the respiration anywhere. Retraction of the head did not increase the cyanosis. The Roentgen ray showed no enlargement of the thymic shadow, but the right lung was not quite as clear as the left.

Baby G., seen when it was thirty-two hours old, was delivered by cesarean section shortly before term. It was in good condition when born, breathed at once, but did not cry. The respiration was rapid from the first. It quickly developed attacks of cyanosis. At times it cried vigorously. It had been kept in a padded crib with heaters and had had oxygen during the last twenty-four hours.

The color was good, except for jaundice. The respiration was about 70 and very superficial. There was some retraction of the supraclavicular and suprasternal spaces. The heart was normal. There was slight dulness in the lower two thirds of the right back and respiration was not as loud in the right back as elsewhere. There was no change in the character of the respiration. No râles were heard.

This baby, like the last one, did very well, all symptoms ceasing in a few days.

Baby M. was seen when twenty-two hours old. It was born at full term after an easy breech labor and cried quickly. It weighed, however, only 4 pounds and 2 ounces. It began to be cyanotic when about five hours old. The cyanosis had continued, but had diminished somewhat. It had been having oxygen freely. The temperature was normal.

It was small and poorly nourished. There was marked general cyanosis. The throat was normal. The heart sounds were normal. The cry was very feeble. Percussion was everywhere a little dull. Respiration was rapid and superficial. The respiratory murmur was feeble, but air entered both sides alike. A moderate number of moist râles were heard on both sides, back, and front. There was no dulness under the manubrium. The thymus was not palpable. There was no retraction with inspiration and the diaphragm apparently moved on both sides. The baby died in a few days.

Congestion of the lungs resulting from a congenital heart lesion may give the symptoms and physical signs of atelectasis of the lungs. In the following instance congestion of the lungs

due to a very large patent ductus arteriosus, which gave no physical signs, was mistaken for congenital atelectasis.

This baby was delivered by cesarean section at term before labor began. It weighed 7½ pounds. It cried hard at once, but had a good deal of mucus in the throat. Three hours later it became cyanotic and began to have a whining cry. The cyanosis continued intermittently. At the beginning of the cyanosis the temperature was about one degree below normal, but with heaters had been kept since then a degree or so above normal. The baby was seen when twenty-nine hours old.

It was a little pale, but not cyanotic. The mouth and throat were normal. The heart was normal. There was a short inspiration with marked retraction of the epigastrium and very little motion of the chest, then a rather longer expiration with a whining cry. Air did not enter the backs well, especially on the right. A very few fine râles were heard on the left. There was no change in the percussion note.

The baby died a few hours later. The autopsy showed a very large ductus arteriosus, the duct being larger than the aortic or pulmonary artery. As the result there was a tremendous congestion of the lungs which caused the respiratory symptoms and accounted for the physical signs of atelectasis.

Cerebral Hemorrhage.—Although cerebral hemorrhage is one of the most common causes of disturbances of the respiration in the first few days of life, these symptoms are usually less prominent than many of the other manifestations of cerebral irritation or increased intracranial pressure. Occasionally, however, they are the first symptoms to appear. They are more likely to occur when the hemorrhage is below the tentorium. The respiration is never noisy as the result of cerebral hemorrhage. It may be either diminished or increased in rate. Irregularity is the most characteristic change and may be very marked. The following are instances of intracranial hemorrhage in which the respiratory symptoms appeared early and were quite prominent.

Baby A. was born after a very hard labor, but was resuscitated quickly and cried well. It seemed all right until it was about six hours old, when the respiration became irregular and gasping in character. The baby was also a little dusky from time to time. It developed a slight internal strabismus on the right as well as slight ptosis on the same side. The respiration continued practically the same, at times, however, becoming quite difficult. In the attacks it was somewhat rigid. It was seen when thirty-six hours old.

It was slightly cyanotic. The fontanel was slightly depressed. The pupils were equal and reacted to light. There was a facial paralysis on the right. There was slight general rigidity. The knee-jerk was exaggerated on

the right, but was not obtained on the left. There was no Kernig's sign. It had repeated attacks during the examination in which it became rigid, twitched a little, retracted the head, and breathed peculiarly.

A lumbar puncture was done and about 3 c.c. of slightly blood-tinged fluid, under low pressure, allowed to run off.

The baby was at death's door for nearly a week, but two months later was perfectly normal in every way.

Baby G. was born at full term after a very hard low forceps delivery. It was in a condition of pallid asphyxia. It was at least an hour before it began to breathe. Slight paralysis of the left side of the face was noted at birth. It moaned and fretted during the next twelve hours. It then began to hold its hands in the position of tetany and a few hours later refused to swallow and began to have slight attacks of spasm of the face and irregular respiration. These attacks lasted from one half a minute to ten minutes. When twenty-four hours old it had a convulsion. It was seen soon after.

It was unconscious. The anterior fontanel was bulging, tense, and pulsating. The pupils were very small and did not react to light. There was no facial paralysis. There was slight rigidity of the legs and more of the arms and hands. The knee-jerks were not obtained. There was a slight Kernig sign on both sides. There was moderate cyanosis, which increased on handling. It stopped breathing temporarily several times during the examination. The rectal temperature was 96.6° F.

The baby was so ill that it seemed useless to do anything for it. It died twenty-four hours later.

Prematurity and Congenital Debility.—Rapid respiration, which is also often irregular, is not uncommon in premature and congenitally feeble infants. There are, of course, no physical signs of abnormality in the respiratory tract, only the evidences of prematurity and general muscular weakness. Congenital atelectasis is often a complication. The increase in the rate of the respiration in premature infants is due in part to the imperfect development of the pulmonary alveoli and in part to deficient expansion of the chest as the result of muscular weakness; in congenitally feeble infants it is due chiefly to muscular weakness. Irregularity in the rhythm is due in both premature and congenitally feeble infants to imperfect aëration. Incomplete development of the respiratory centers at birth also plays a part, especially in premature infants.

Congenital Malformations.—Other less common causes of disturbances of the respiration, manifesting themselves at birth, are congenital malformations. They are usually of the respira-

tory tract, but may be elsewhere. I shall not attempt to enumerate them all, but shall merely mention a few examples of such abnormalities which I have seen.

Cyst of Throat.—Baby K. seemed all right at birth, although the labor had been a difficult one. It was noticed that, from the first, he had more mucus in the mouth and throat than usual. When two days old he turned blue while nursing. It seemed hard for him to breathe. He continued to have attacks of difficult breathing all that day. That afternoon he had a little twitching of the left face before the spells. It was necessary to take him off the breast because of the difficulty in nursing. He even choked a little when water was given. He was seen when three and a half days old.

His color was good. At times there was slight twitching of the face and occasionally of the whole body. After many of these twitchings he became a little blue and breathed irregularly. The fontanel was depressed. There was no rigidity, except in the attacks. There was no paralysis. The knee-jerks were not obtained. There was no Kernig's sign. The mouth and throat were not examined because the obstetrician said that he had examined them and they were normal. The lungs were clear. The thymus was not palpable and there was no dulness under the manubrium. The probable diagnosis was a slight cerebral hemorrhage.

The baby died three days later. Lumbar puncture showed fluid perfectly clear without any pressure. The doctor felt in the throat after death and found a tumor the size of a horse chestnut in the right side of the pharynx, low down.

The moral to be drawn from this case is, of course, that in all cases of difficult respiration in infancy or childhood a digital examination of the throat should be made. Inspection is not sufficient. I have also seen several cases in which a cyst at the root of the tongue caused noisy and difficult respiration. Such cysts are usually not visible, but have to be felt with the finger. In several other instances a congenital macroglossia has interfered with normal breathing.

Congenital Atresia of the Esophagus.—The symptoms of congenital atresia of the esophagus are at first mainly respiratory, because the newborn baby is unable to swallow the amniotic fluid and secretions in the nasopharynx. The true condition is almost never suspected during the first few days and the trouble is supposed to be a catarrhal condition of the nasopharynx. It is only after the milk comes in and the baby begins to vomit that suspicion as to the true condition is aroused. The following histories illustrate this point:

Marjory D. seemed normal at birth, except that there was much mucus in the nose and throat which was removed with considerable difficulty. There continued to be a profuse discharge of mucus which, at times, accumulated and caused severe suffocative attacks relieved only by the mechanical clearing of the nose and throat. There was a constant rattling in the nose and throat between these attacks. Her cry was somewhat feeble and a little hoarse. Her mother's milk had appeared on the third day and seemed sufficient in quantity. She took the breast well, but was liable to have an attack of suffocation come on while nursing. At times she vomited during or immediately after nursing; at others she apparently retained several successive feedings without vomiting. She was seen when four days old.

She was sleeping quietly, but with a little rattling in the nose. Closing the mouth did not interfere with breathing or wake her up. A probe was easily passed through both nostrils. When the tongue was depressed a large amount of yellowish white liquid mixed with mucus came up in the throat. When this was cleaned out and the operation repeated, more of the same material appeared. Palpation of the throat showed nothing abnormal. Her cry was a little hoarse, but strong. The heart and lungs were normal. There were no evidences of any disease of the nervous system.

John G. was also seen when four days old. He was blue and much choked up at birth. He seemed filled up with mucus. It was hard to get him started breathing. Since then he had had frequent attacks of choking and blueness. He seemed to fill up with mucus and then to have a blue spell, get rid of it, and then be of good color until the next spell. He had been put to the breast regularly. It had not been appreciated that he did not suck or get anything until the day before, when the milk came in. It was then found that he nursed very little and spit up at once what he did take. He became choked and blue as soon as he began to get anything.

When seen he was of good color. He soon had a choking spell, however, during which he became extremely blue, got up a little mucus, then quieted down again. Examination was otherwise negative. A catheter, passed through the mouth, met a definite obstruction about 17 cm. from the gums. He died six days later.

Congenital Malformations of the Diaphragm.—The symptoms of congenital malformations of the diaphragm are very largely respiratory. The following is an example of what, to me at least, is a unique condition:

Allen K. was seen when three and one-half months old because of marked malnutrition. His parents had thought nothing about his peculiar breathing. When questioned, however, they said that the baby had always breathed badly. They thought that he had cried out loud during the first six weeks, but since then had not been able to. They said it was hard for him to take the bottle because of the trouble with the breathing. When disturbed or excited he sweat profusely and got a little blue.

He was much emaciated. He was pale, with, at times, a little tinge of

cyanosis. The fontanel was deeply sunken. The bones overlapped at the sutures. Nothing abnormal was seen or felt in the throat. He could make only a little croaking cry. The chest moved excessively in respiration. The whole abdomen sank in and the epigastrium went up into the chest. There was no rosary. The heart was normal. The thymus was not palpable. There was no dulness under the manubrium. The cry was not like that of laryngismus stridulus. When he became at all excited, he got somewhat cyanotic and perspired profusely.

Fluoroscopic examination showed nothing abnormal about the trachea, bronchi, or lungs, but complete paralysis of the diaphragm on both sides.

The severity of the respiratory symptoms in congenital diaphragmatic hernia varies materially from time to time, depending upon the size of the hernia at different times. They may or may not be present at birth. The rate of the respiration is increased. There may be difficulty in both inspiration and expiration. The respiration is not noisy.

The physical signs are most confusing and misleading and are quite likely to be misinterpreted. When well marked, however, they are quite characteristic and differ from those in any other condition. The affected side is often somewhat enlarged. The heart and mediastinum are displaced toward the normal side. The percussion note may be flat, dull, normal or more or less tympanitic, according to whether the intestines or the lung are next to the chest wall and whether the intestines contain feces or gas. The respiratory sound is always diminished on the affected side, and sometimes absent, according to the size and position of the intestines with relation to the lung. It is usually normal in character, but may be bronchial, if the lung is compressed. The voice sounds vary in the same way as the respiration. Tactile fremitus is usually diminished. Gurgling sounds, not unlike those made in the intestines, may be heard. Most characteristic, however, is that the combination of physical signs is not consistent with that given by any of the pulmonary diseases. Diaphragmatic hernia should always be recognizable by the physical signs. I know from experience, however, that it is easy to overlook it. The diagnosis is easily confirmed by a roentgenogram of the chest. The picture is clearer, if an opaque meal is first given. The following case is of interest in that the symptoms were so late in developing:

This baby was born a month ahead of time, but appeared normal at birth. She had bronchopneumonia when four months old, but had otherwise been well and flourished until she was seventeen months old. She then had an attack of vomiting and diarrhea lasting for two or three weeks. At this time and afterward it was noted that she was short of breath, especially on exertion, and that she had attacks of coughing with vomiting. She was seen when eighteen months old.

She was well developed and nourished and did not appear ill. The left chest, however, bulged a little in the region of the nipple and axilla. The heart was displaced 2 cm. to the right. There was impaired resonance over the whole left chest, except at the apex. The breath sounds were diminished in intensity, but normal in character. A diagnosis of pleural effusion had been made and the chest had been tapped, but no fluid obtained. Roentgenograms after an opaque meal showed, however, that there was a diaphragmatic hernia. Auscultation later, after massage of the abdomen, revealed intestinal gurgling in the chest.

Amyotonia Congenita.—Another unusual cause of respiratory disturbance in infancy is amyotonia congenita. This disease is seldom recognized during the first few weeks or months of life, and the respiratory disturbances, like the weakness of the extremities, either overlooked or attributed to debility. The intercostal and accessory muscles of respiration are likely to be involved with the other skeletal muscles, but the diaphragm almost always escapes. Respiration is, therefore, largely diaphragmatic. It is usually rapid. The thorax moves but little. As the result of the pull of the diaphragm on the chest wall, the inability of the external muscles to expand the thorax, and atmospheric pressure deformity of the chest results. The sides of the chest sink in and the sternum is pushed out in front so that the ribs leave the sternum at but little more than a right angle. The deformity resembles that sometimes seen in rickets, but is more marked than it is in any but the most serious cases of rickets. The cry is usually feeble, because the baby has so little breath with which to cry. The small brother of one of my patients with amyotonia congenita said that it sounded "like a sick kitten." This feebleness of the respiratory muscles predisposes to respiratory infections, which are the usual cause of death in this disease.

Congenital Malformations of the Heart.—Dyspnea is a very constant symptom in congenital malformations of the heart and

great vessels, although in many cases it is not noticeable when the infant is at rest. It is usually accompanied by and varies directly with the degree of cyanosis. It is the cyanosis which usually attracts attention and the dyspnea is overlooked or its importance not appreciated. Not infrequently, however, there is more or less dyspnea without cyanosis. In such instances, if no cardiac murmur is heard, the real cause of the dyspnea is not suspected.

Peculiar attacks of suffocation are not uncommon in congenital malformations of the heart. They are always associated with marked cyanosis. They are usually started by coughing or crying and last from five to fifteen minutes. Consciousness is lost and a convulsion occurs occasionally. When there happens to be no cardiac murmur these attacks are almost always attributed to some other cause, usually the thymus. A careful physical examination and analysis of the symptoms between attacks should, however, prevent such mistakes.

Another cardiac cause of dyspnea in infancy is *idiopathic hypertrophy of the heart.* This condition is certainly in many instances, and probably in all, congenital. The etiology is unknown. The heart is enormous, the enlargement being mostly to the left. It fills up a large part of the lower left chest, thus compressing the left lung. This is probably the chief cause of the dyspnea, although the diminished mobility of the left chest because of the enlarged heart may play a part. The physical signs are pathognomonic, but are almost certain to be misinterpreted, unless the physician is familiar with the condition. The left chest is enlarged and its movement diminished. There is flatness or dulness in the left front and axilla, due in part to the large heart and in part to the compressed lung. The respiratory murmur is diminished and is bronchial or bronchovesicular. The tactile fremitus is diminished and there is a marked sense of resistance. There are no cardiac murmurs and the right border of the heart is further to the right than normal. I am inclined to think that every honest man will admit that the first time that he saw a case of this sort he made a diagnosis of fluid in the left pleural cavity and stuck in a needle. The

diagnosis is easy, however, if the condition is kept in mind. It is easy to confirm it with a roentgenogram. The following case is an example:

This boy weighed 8 pounds at birth and seemed normal in every way until he was six months old. He then began to take his food poorly and to have crying spells. When he was thirteen months old it was noticed that he was anemic and yellow, and that he was short of breath and at times a little blue. Soon after that he began to have occasional attacks of coughing, dyspnea, and tachycardia. It was also noticed that his heart was always rapid. He had gained slowly and had not sat up alone or walked. He was seen when seventeen and a half months old.

He was well developed, but poorly nourished. He was pale with a yellowish tinge. The respiration was 70. The precordia was quite prominent, especially on the left. The cardiac impulse was lower down and further to the left than normal. A slight diastolic murmur was heard over the whole precordia. The whole left chest was markedly dull and no respiratory sound was heard on the left side, either back or front. There was no enlargement of the liver or spleen. The hemoglobin was 40 per cent., the red cells 2,200,000, and the white cells 13,000.

A diagnosis of pulmonary effusion on the left side had been made and two thoracenteses done. A little bright blood had been obtained each time.

He died twenty-four hours later. The pericardium contained a little blood. The heart was very much enlarged, weighing 200 gm. The heart wall showed where it had been punctured, but there was no leakage. There were only two aortic valves, but there was no leakage. No adequate cause for the cardiac enlargement was found. The left lung was very small and atelectatic throughout.

Idiocy, especially Mongolian, is another cause of continuously irregular or peculiar respiration in infancy. It is often associated with adenoids or slight malformations of the nasopharynx and palate, which increase the symptoms. There is nothing pathognomonic about the disturbances of respiration due to idiocy. It is hardly necessary to give illustrative cases, as the cause is evident enough.

Rickets is probably the most common cause of continuously rapid respiration in infancy. When the rate is but little increased, the trouble is simply weakness of the intercostal and other thoracic muscles of respiration, in common with that of the musculature as a whole, which prevents the complete expansion of the chest and thus makes it necessary for the baby to breathe more often. When the rate is increased, there are

usually rachitic deformities of the chest which interfere still more with its expansion. These are due to the pull of the diaphragm on the soft ribs and atmospheric pressure. The most common are retraction at the level of the insertion of the diaphragm—Harrison's groove, flattening of the sides of the chest, and protrusion of the sternum—pigeon-breast. In the severest cases there is almost always a strip of atelectatic lung beside the vertebral column behind on both sides, which makes aëration still more difficult and the respiration more rapid. There is nothing characteristic about the respiration in rickets. The rate is simply increased. The relation between inspiration and expiration is not changed. There is no retraction of the intercostal and other spaces, unless there is also some interference with the entrance of air, as from adenoids. The respiration is quiet, not noisy.

Infantile Paralysis.—An occasional cause of continuously rapid or abnormal respiration is weakness of the respiratory muscles as the result of infantile paralysis. The weakness may be unilateral or bilateral. In either case deformities of the chest may develop, causing further trouble. In one instance in which the difficulty with respiration was unilateral, there was paralysis of the left half of the diaphragm. It is obvious what the physical signs would be. The diagnosis was proved by examination with the fluoroscope.

Laryngitis.—The most common causes of noisy and difficult respiration coming on acutely are catarrhal and diphtheritic laryngitis. It hardly seems necessary to describe the symptoms of these diseases. It should be remembered, however, that the difficulty in respiration is always inspiratory and that, if severe, it is accompanied by retraction of the supraclavicular and lower intercostal spaces, and finally of the epigastrium and lower chest. The noise in breathing is also always in inspiration and is accompanied by hoarseness of the voice or aphonia.

Tracheitis.—An unusual disease, but one which presents a most characteristic picture is acute streptococcus tracheitis. The following history is a typical one:

This boy of four years at first had the symptoms of an ordinary catarrhal laryngitis. After a few hours, however, he began to have difficulty with both inspiration and expiration. The throat was slightly reddened. The larynx seemed to be free. There was no cough and the lungs showed nothing abnormal. Various measures undertaken to relax the spasm gave no relief. A tracheotomy was of no value in relieving the symptoms. During inspiration there was marked retraction of the sternum. During expiration there was a powerful contraction of the abdominal muscles in the effort to force air out. The color remained good until almost the last. Death occurred within twenty-four hours, apparently from cardiac failure due to the exertion of breathing.

It is noteworthy that in this disease there is trouble in both inspiration and expiration, the throat is negative, the cough is not laryngeal, inspiration is not noisy, the voice is clear, the lungs are normal.

Retropharyngeal Abscess.—Still another cause of difficult respiration, which is sometimes noisy and sometimes not, is retropharyngeal abscess. The following case is an example of the usual type:

A baby, five months old, had a "cold in his head." A week later he began to swallow with difficulty. A day or two later it was noticed that he kept his mouth constantly open and could not breathe through his nose. He was seen a week later. He was then taking almost no food and was unable to breathe at all with his mouth closed. He had lost much weight and strength. Both inspection and palpation showed a bulging of the left side of the pharynx, most marked in the upper portion, almost filling the throat. Incision let out about two teaspoonfuls of pus and afforded almost instant relief.

A retropharyngeal abscess is often overlooked because it is not thought of. Another reason that it is often overlooked is that inspection of the throat is trusted and palpation omitted. Inspection, however, is often insufficient, and may lead to grave errors in diagnosis. In the majority of cases the tumor is visible, but not infrequently, especially if low down, it cannot be made out. It can always be felt, if present, although if it is situated low down the finger must be introduced very deeply. In no case in which the symptoms in any way suggest a retropharyngeal abscess should palpation of the throat be omitted.

Asthma.—A much more common cause of difficult respiration in infancy and early childhood than is generally appre-

ciated is asthma. Few physicians realize, apparently, that, after the first year, asthma has to be always kept in mind when there is an acute disturbance of the respiration. The symptomatology is the same as in older children and adults. In making the diagnosis it must be remembered that the voice is clear and that the difficulty is expiratory, not inspiratory. The rate of the respiration is not only not increased, but is often diminished. It is "wheezy." The respiratory murmur is diminished in intensity, but not changed in character. Many râles are heard.

Acute Dilatation of the Stomach and Abdomen.—Acute dilatation of the stomach from either gas or fluid or of the abdomen from gas in the intestines, by pressing up the diaphragm and interfering with its motion, may cause marked dyspnea and cyanosis. In such cases, of course, the cry is clear, the relation between inspiration and expiration is unchanged, and there are no evidences of obstruction. The following case is an example:

A baby of two months, that had been recently weaned and fed on a very strong milk mixture, suddenly became very ill with very rapid respiration and a temperature of 106° F. It was pale and seemed in a condition of severe shock. The physical examination was negative, except that the abdomen was much distended. It had not vomited, but had had very many loose, slimy stools. Its food was stopped and it was given several enemas with relief of the distention. The temperature quickly came down to normal and all the symptoms disappeared. Forty-eight hours later, however, it had a recurrence of the symptoms, the temperature going up to 108° F. It was seen at that time.

The baby was staring. The pupils were a little dilated and did not react to light. The fontanel was depressed. There was no rigidity of the neck. The throat and ear-drums were normal. Respiration was between 60 and 70 and superficial. The heart and lungs were normal. The abdomen was much distended, especially in the upper portion. There were, however, no signs of masses or fluid and no localized spasm. The legs were a little rigid, so that it was impossible to tell about Kernig's sign or to obtain the knee-jerks. There were no evidences of enlargement of the thymus. The urine, obtained by catheterization, showed nothing abnormal. Roentgenograms of the chest showed nothing abnormal in the lungs or in the size of the thymus.

Repeated enemas were given, with relief of the distention. The symptoms all disappeared at once and the temperature came down to normal. The baby was put on breast milk and had no return of the rapid respiration or other symptoms.

"Breath-holding" and Laryngismus Stridulus.—Sudden attacks in infancy in which respiration stops temporarily are the result of either "breath-holding" or laryngismus stridulus. The latter is one of the manifestations of spasmophilia. The symptoms of an attack are pathognomonic. The baby makes several short inspirations in rapid succession, each one accompanied by a crowing sound. It then stops breathing with the chest in full inspiration. It quickly becomes cyanotic. After it becomes sufficiently narcotized the spasm relaxes and it begins to breathe again. In rare instances it does not breathe again and dies. Occasionally an attack terminates in a convulsion.

Babies who have attacks of laryngismus stridulus always show other signs of spasmophilia. They are quite likely to have carpopedal spasms—tetany—as well as attacks of laryngismus stridulus. Either Trousseau's sign or the facial phenomenon, or both, can almost always be elicited. Erb's phenomenon is also always present and the blood shows a diminution in calcium. None of these things are present in "breath-holding." This condition is more common in older children than in infants. The holding of the breath is not preceded by inspiratory crowing, but is almost invariably precipitated by crying or anger. There are, moreover, no other manifestations of spasmophilia.

New Growths in Larynx.—Even in early childhood a new growth in the larynx may be the cause of chronic, noisy, and difficult respiration. The following case is an example:

This little girl was seen July 1st when three years old. In March she had a cold and her voice became husky. The huskiness continued and six weeks before she was seen she lost her voice so that she could only whisper. She was able to lie down at night, but her breathing was noisy. At times she "fought for breath." She was never blue. She had had very little cough. There had been a little fever on several occasions, but the temperature had not been taken regularly. She had lost 3 pounds in the last three weeks.

She was poorly developed and nourished and moderately pale. The throat was generally a little reddened and edematous. She could not speak or cry aloud. When quiet, the respiration was not audible. When she was a little excited, it became noisy, the difficulty being in inspiration. When she was breathing quietly, there was no retraction, but, when she was excited or crying, there was retraction of the lower intercostal spaces. There was no dulness under the manubrium and the thymus was not palpable. There was

bronchial respiration over the dorsal spines down to the middle of the back. There was no interscapular dulness. The lungs were normal. The character of the respiration, however, was everywhere changed. Air entered both sides alike, but when she was crying or excited, laryngeal wheezing could be heard over the whole chest, back and front. Roentgenograms showed no enlargement of the thymus, no enlargement of the tracheobronchial glands, and no foreign body, but a little emphysema of the lungs on both sides. Examination with the laryngoscope showed a papilloma of the larynx.

It is noteworthy that, as in almost all cases of laryngeal obstruction, the difficulty was entirely in inspiration and the voice was affected.

Syphilis of Larynx.—In some instances, however, there is interference with both inspiration and expiration, as was the case in the little boy of seven and a half years with syphilis of the larynx, whose history follows. Incidentally, syphilis of the larynx is an exceedingly rare condition in childhood.

He began to lose his voice eight weeks before he was seen, the voice gradually becoming a whisper. Six weeks before he was seen, he began to have attacks of severe dyspnea and cyanosis at night. He never had more than one attack in a night and never had any during the day. He coughed and vomited at the end of the attacks.

He was well developed and nourished. There was obstruction to both inspiration and expiration. He could not talk aloud. Pressure on the larynx caused some pain and increased the obstruction. The nose, ears, pharynx, and tonsils were normal. Both sides of the chest moved alike. There was retraction of the suprasternal notch and of the epigastrium. The lungs were resonant. Inspiration and expiration were both prolonged. High pitched râles were heard throughout both chests. Laryngeal examination showed a round mass projecting from the right side of the larynx immediately above the vocal cord and concealing it. The surface was red and slightly granular. There was slight swelling of the mucous membrane of the posterior and lower walls of the larynx. The aperture of the glottis in inspiration was about 1/10 inch. Under treatment with iodid of potash the tumor rapidly diminished in size and finally disappeared.

Foreign Bodies.—A foreign body in the lower air-passages may be the cause of respiratory disturbance in infancy and early childhood. Cough, often occurring in paroxysms, is a frequent accompaniment of the rapid respiration. A foreign body cannot be ruled out as the cause of the symptoms because there is no history of its being inhaled. A baby may have inhaled it when no one was about and, of course, is unable to tell about it. Fur-

thermore, months may elapse after a foreign body is inhaled before symptoms develop and everyone may have forgotten a fleeting attack of respiratory spasm or disturbance in the past. There is nothing pathognomonic about the respiratory disturbances resulting from a foreign body, although paroxysms of coughing are suggestive. The rate of the respiration is increased, but it is not noisy, and the relation between inspiration and expiration is not changed. The physical signs are, however, almost always unilateral, because a foreign body which is small enough to pass through the larynx is usually small enough to pass through the trachea also and into a bronchus, usually the right. They must necessarily vary, according to whether the bronchus is partially or entirely closed and how much damage has resulted in the lung from imperfect drainage and aëration and secondary infection. Roentgenograms will often help to verify the diagnosis. It must be remembered, however, that roentgenograms show only bodies which are opaque to the Roentgen rays. This is shown in the following instance:

A baby two years old was eating dried figs and playing with nails. It had a sudden attack of coughing and choking. The next day it coughed up a piece of fig and developed high fever and continuous cough. It was seen four days later. There was diminished respiration and râles over the whole left side. Roentgenograms showed nothing abnormal. Bronchoscopic examination a few days later showed marked swelling of the mucous membrane of the left primary bronchus with a discharge of mucopus. No foreign body was seen.

During the next three weeks more and more air entered the left chest, but definite dulness and bronchial respiration developed in the left back below the middle of the scapula and extending from the median line to the posterior axillary line. A few days later the breath began to have a fetid odor. During all this time the temperature, pulse, and respiration had been high and the baby had been fed with a tube, because it refused to swallow. It was operated on a month after the onset, 1½ inches of the eighth rib on the left being removed. A gangrenous area, well walled off, was opened and drained. The baby died, however, four days later.

A boy of eight years began to have fever and cough eleven days before he was seen. The fever lasted for a few days, but the cough continued. Three days before he was seen he had a chill and the temperature went to 104° F. Since then it had continued in the neighborhood of 103° F. His cough had increased and he complained of occasional pains in the right shoulder.

His cheeks were flushed, but he did not seem very sick. The ears and throat were normal. He had a frequent, short cough. There was dulness with diminished respiration and voice sounds in the right back and axilla, below the angle of the scapula behind and the midaxilla in the side. The tactile fremitus was unchanged. There was no change in the character of the respiration and voice sounds. A probable diagnosis of lobar pneumonia was made, although other pulmonary conditions were considered as possibilities. He improved after a few days and the temperature dropped to normal. His cough continued, however, and the signs in the lungs did not entirely clear up. Roentgenograms showed a spear-shaped shadow at the root of the right lung. The metal end of a "top", which was the cause of the shadow, was removed from the bronchus about three weeks later. The boy then said that he had it in his mouth while at the movies about six months before and swallowed it.

Mediastinal Tumors.—Continuous, chronic disturbance of the respiration may be due to pressure on the trachea, either in the neck or inside the thorax, from the outside. Pressure from enlargement of the thymus has already been described. Other possible causes are enlargement of the isthmus of the thyroid, new growths, and abscesses in the mediastinum. In such cases, although both inspiration and expiration are usually affected, there is almost always more trouble with inspiration than expiration. The respiration may or may not be noisy, according to the amount of pressure and consequent narrowing of the lumen of the trachea. The voice is usually feeble, but is clear. There are no signs in the lungs, unless they are also involved, except diminished respiration on both sides and râles from retained secretions. The following cases are examples of some of these rare conditions:

A little girl, two and one-half years old when she was seen, began to have a "croupy cough" in August. This cough continued intermittently until she was seen early in February. It varied in severity. Roentgenograms taken about a month after the onset showed no enlargement of the thymus. She had had some difficulty in breathing during the twenty-four hours before she was seen, the trouble being present both day and night.

Her color was good. There was no nasal discharge. The tonsils were large, but not inflamed. The voice and cry were clear. Inspiration and expiration were both a little noisy. Expiration was somewhat prolonged. There was slight retraction of the supraclavicular and lower intercostal spaces with inspiration. There was an elastic swelling about $\frac{3}{4}$ inch in width and $\frac{1}{4}$ inch thick over the trachea at the seat of the isthmus of the thyroid. The

finger could be introduced below this swelling and above the manubrium. No tumor could be felt in the suprasternal notch and there was no dulness under the manubrium. The bronchial voice sound did not extend below the seventh cervical spine. The lungs were normal except for many sibilant and sonorous râles. A probable diagnosis of a cyst of the thyroid was made. Operation was advised, but refused.

A boy began to have swollen eyelids about February 1st, when he was three and one-half years old. The swelling continued off and on, but varied in amount. About the same time enlarged veins were noticed in the neck. About April 1st he began to make a noise on breathing and to get out of breath on exertion. The difficulty with breathing increased so that he was unable to sleep lying down. Cough began April 11th. He had never had a bad attack of suffocation and the onset of the difficulty in breathing was quite sudden. He was seen April 14th.

He was well developed and nourished. The throat was normal. The upper chest seemed a little full. The superficial veins of the upper front chest, as well as the veins in the neck, were enlarged. In addition to the dark blue veins there was a semicircle of fine, bright red veins over the manubrium. There was flatness on percussion over the sternum and extending just above the sternum. An indefinite swelling could be felt above the sternum. The flatness extended into the right chest above the fourth rib. There was a little resonance over the extreme apex and outside. There was dulness between the scapulæ and over the spinous processes to the fourth dorsal spine. The spoken and whispered voices were bronchial and the respiration was bronchial through the fourth dorsal spine. Less air entered the right lung than the left. The respiration over the dull area on the right was bronchial, as was the voice sound. Wheezing râles, apparently made in the larynx, were heard over both sides. The voice was clear. The heart was in normal position. There was slight general cyanosis, especially on reclining. Inspiration was a little noisy. Roentgenograms showed that the heart was in normal position. There was a shadow in the mediastinum, which appeared wider than normal, and a round shadow extending into the upper right chest, nearly filling it.

The diagnosis of sarcoma was made. He died in a short time.

I have seen a number of cases of abscess in the anterior mediastinum in hospital practice, all due to the breaking down of tuberculous glands. Unfortunately, I am unable to find the records of these cases. The most striking thing in all of them, however, was the picture shown by the Roentgen ray. In all of them there was a sharply outlined shadow, shaped like an egg or a sausage, under the sternum. I have never seen such a picture in any other condition.

Tracheobronchial Adenitis.—The tracheobronchial lymph-nodes may be sufficiently enlarged to cause enough pressure on

the trachea or bronchi to cause dyspnea and coughing. In such cases the enlargement is almost invariably due to tuberculosis. Occasionally the respiration is noisy, more often "wheezy," but still more often quiet. Inspiration and expiration are usually both involved. Theoretically, expiration should be affected more than inspiration, because the chest is smaller in expiration than in inspiration and, therefore, the pressure on the trachea is greater. Practically, it is only occasionally that any difference can be noticed. The head is sometimes held hyperextended. There is often cough in addition. There is usually nothing characteristic about it. It is almost always dry. Sometimes it is very persistent and occasionally paroxysmal, resembling very much that of whooping-cough.

The physical signs are usually quite definite. There is dulness over the upper dorsal spines and in the more marked cases interscapular dulness. The voice, whisper, and respiration are bronchial below the first dorsal spine, the distance down which they extend depending upon the amount of enlargement. D'Espine's sign is present. If the pressure is exerted on the trachea alone, respiration is diminished in intensity in both lungs. If it is exerted more on one bronchus than on the other, it is diminished on that side. It is not changed in character. If the pressure is sufficient to cause atelectasis of the lungs or secondary bronchopneumonia from retained secretions and infection, there will be the signs of partial consolidation of the lungs, with râles, on one or both sides behind. These signs are usually unilateral, because the enlargement of the glands, if marked, is usually greater on one side than on the other. Roentgenograms are very useful in confirming the diagnosis. Bronchoscopy is usually not necessary, but may be most helpful in both diagnosis and treatment. Occasionally one of these nodes breaks down and the abscess formed extends further into the lumen of the bronchus and increases the symptoms. Finally the abscess may break into the bronchus, causing still more marked symptoms and physical signs. I have seen a considerable number and variety of cases of this sort. The following history is a good example of a severe case:

Seven months before he was seen, when only three years old, this child had a cold with difficult breathing and cough. During the last two weeks the difficulty in breathing had increased materially and wheezing had developed. The cough had increased. There was no expectoration. At times, especially at night, he had difficulty in getting his breath and became blue. The breathing had become considerably more noisy in the last few days.

He was well developed and nourished and of fair color. Inspiration was somewhat noisy. The tonsils were cryptic and reddened, the pharynx filled with mucus. The bronchial voice extended to the fourth dorsal spine. Both sides of the chest moved alike. There was a little retraction of the abdomen with inspiration. Air entered both sides of the lungs alike and the breath sounds were vesicular. There was no disturbance of the relation between inspiration and expiration. Many medium and coarse moist râles were heard on both sides, back and front. The Roentgen ray showed some widening of the shadow at the base of the heart. The tuberculin test was very strongly positive.

Two days later there was much greater interference with inspiration and marked pulling in of the lower ribs. Air entered the left side better than the right. There was spinal dulness as well as bronchial voice to the fourth dorsal spine. The symptoms all gradually increased. Dulness developed to the right of the upper dorsal spines and the diminution of respiration on the right side increased. Two weeks later roentgenograms showed a dense shadow on the right extending from the level of the fifth dorsal vertebra to the diaphragm, two-thirds of the way to the chest wall, in a roughly fan-shaped manner, the densest part of the shadow being at the hilus and becoming less dense as it spread out.

Under rectal anesthesia the smallest size bronchoscope was used, and a mass, probably the wall of a tuberculous cavity, sucked out, as well as much detritus. This detritus was examined and found to contain tubercle bacilli.

Two weeks later the chest was entered through the eighth and ninth ribs in the right back, close to the spine. A mass of glands varying in size from that of a robin's egg to that of a pigeon's egg was felt around the bronchi. A small mass of glands was removed, but the condition was so bad that the operation was given up. He breathed more easily after the operation, but died in about twenty-four hours from circulatory failure.

There are many other causes of rapid, difficult, or noisy breathing in early life which might be mentioned. Among them are adrenal hemorrhage in the first days of life, pericarditis, chronic bronchopneumonia, chronic interstitial pneumonia, and mediastinitis in childhood, and acute and chronic diseases of the peritoneum and the abdominal organs in both infancy and childhood. There is one more disease, however, which should be taken up in more detail, that is, meningitis, especially pneumococcus, in which in infancy the earliest and most marked

symptom may be rapid respiration. The following case is an example:

Meningitis.—This baby, eight months old, began to be uncomfortable and fussy early in the morning of February 14th. The temperature was 102.5° F. He was fussy all day, but took his food well. He did not vomit and his bowels moved. He had a comfortable night. The temperature the morning of the 15th was 104° F. He took his food well, did not vomit, and his bowels moved. He had no cough. In the afternoon his respiration became very rapid. It probably had been before, but had not been particularly noticed. He was seen at 3 P. M. He was conscious. The pupils were equal and contracted from paregoric. The fontanel was level. There was no rigidity of the neck or neck sign. There was no spasm or paralysis of any muscles supplied by the cranial nerves. The ear-drums were normal, as was the throat. The respiration and pulse were rapid. The respiration was not deep or sighing. The lungs were normal. The knee-jerks were equal and normal. There was no Kernig's sign. He was a little twitchy. The rectal temperature was 104.7° F.

The outstanding symptoms were that the baby was evidently seriously ill, that it had a high temperature, and that the respiration was very rapid. Examination with the fluoroscope showed no evidences of pneumonia.

The baby grew rapidly worse during the night. The next morning it showed the typical picture of meningitis. A lumbar puncture showed a cloudy fluid filled with pneumococci.

It is evident that, while there are many more causes of rapid, difficult, or noisy respiration in early life than at first thought would seem possible, the diagnosis between them is not as difficult as their number would make it appear. The symptoms of many of them are pathognomonic. While the others have many symptoms in common, there are enough differences in the histories and physical signs which they present to make the diagnosis between them reasonably simple, provided these diseases are kept in mind and reasonable care is exercised.

CLINIC OF DR. FREDERICK T. LORD

MASSACHUSETTS GENERAL HOSPITAL

A CASE OF DIAPHRAGMATIC HERNIA WITH REMARKS ON DIAGNOSIS

THE following case history is reported because of the rarity of the condition, and the presence of symptoms and physical signs which permitted a tentative clinical diagnosis:

Mrs. L. C., referred by Dr. A. H. Stockbridge of Lynn, fifty-six, a corsétière, has been troubled almost daily for the past ten or twelve years by epigastric distress coming immediately after eating and lasting for about one-half hour. This occurs only after the noon and evening meal. It is not severe. It is relieved by soda. It radiates at times straight through to the back.

For the past two years she has been troubled by a dull, aching pain which starts in the epigastrium and shifts from there to the precordial region with still some pain remaining, however, in the epigastrium. The pain is also referred to the left supra- and infra-clavicular regions. It occurs almost every day and comes on while she is eating. She may have to stop eating on account of it. It lasts from one to one and one-half hours, or until she can pass gas through the bowels. It is not severe enough to double her up, or make her groan, or incapacitate her for work. It does at times keep her awake. It radiates to the back under the left shoulder blade, but not into the shoulder or down the arm. She is not short of breath with it. Exertion is not an exciting cause. It is not aggravated by long breath or bending the spine. Only food seems to be of importance in bringing on an attack. The bowels are somewhat constipated. There is no abdominal distention. The appetite is somewhat impaired. She has much gas. There is no nausea or vomiting. There is no history of jaundice, the vomiting of blood, or of blood in the urine or stool. There is no cough or shortness of breath. She sleeps well and does not get up at night to pass urine. Her maximum weight was 184 two years ago; she now weighs 153. Her height is 5 feet, 10½ inches.

The past history is negative, except for a pleurisy at the age of twenty-five. She was tapped three times. She thinks there was no cough in this attack. There was pain and elevated temperature. She was in bed for seven weeks. A sister is said to have been operated upon for a diaphragmatic

hernia. The family history is otherwise negative. Habits are negative. The catamenia ceased at 44.

On examination she was well developed and nourished. There were dark circles about the eyes. The pupils were equal, regular, and reacted readily to light. There was no sinus tenderness. There was slight cyanosis of the lips. The cardiac impulse was in the fifth interspace about in the nipple line. The heart was not apparently enlarged. The sounds were regular and of good quality. The rate was 84. The aortic second sound was louder than the pulmonic second sound. There was a systolic, rough murmur at the left second interchondral space, not transmitted to the neck. There was no supracardiac or spinal dulness. There were gurgling sounds of peristaltic motions throughout the left front as high as the clavicle and behind to the spine of the scapula. There was slight dulness at the left base behind, below the angle of the scapula, with diminished breathing and without other signs. There was no succussion. Respiratory excursion of the two sides of the chest was the same. The anterior costal margin moved equally and well on both sides. The diaphragm shadow was present and equal on both sides. There was no edema. The reflexes were normal. The blood-pressure was 145/90. The abdomen was negative. The temporal arteries were tortuous. The radials were not hard. The spine was fairly flexible for all motions without pain.

The urine was negative, with the exception of the slightest possible trace of albumin. The blood smear and Wassermann test were negative. The hemoglobin was 80 per cent. The non-protein nitrogen in the blood amounted to 32 mg. per 100 c.c. of blood. A specimen of stool was negative by microscopic examination and the Guaiac test for blood.

Comments on the History.—To judge from the history alone regarding the nature of the disturbance, peptic ulcer is to be considered. The relation of epigastric distress and pain to the intake of food is consistent with this explanation, but the shifting of pain from the epigastrium to the precordium is atypical for ulcer and the radiation of pain to the left supra- and infraclavicular regions is almost wholly incompatible with uncomplicated peptic ulcer.

The distribution of pain and radiation to the left supra- and infraclavicular regions is suggestive also of angina pectoris and this was considered to be the explanation by one physician who treated her accordingly for a period of eight to nine months. The definite relation of the pain to the ingestion of food, its duration, occurrence apart from exertion and absence of shortness of breath are against angina pectoris.

Pain due to irritation of the viscera is often referred to a site remote from the point of irritation. In 11 patients with basal pleurisy in Capps[1] series, pain was referred to the neck region. The maximum points of pain in the neck were generally along the trapezius ridge and the pain was always associated with hyperalgesia. Mechanical irritation of the superior surface of the diaphragm in the course of thoracentesis caused pain in the neck of maximum intensity along the ridge of the trapezius muscle, while irritation

[1] Trans. Assoc. Amer. Phys., 1911, 26, 486.

of the peripheral rim of the diaphragm caused pain in the lower thorax, the lumbar region or the abdomen. Similar experiments by Capps[1] made in the abdomen after the injection of sterile air showed that irritation of the marginal regions of the inferior surface of the diaphragm gave rise to pain over the corresponding hypochondrium and caused pain in the neck.

Pain referred to the region of the neck is at times observed in patients with lesions of the diaphragm. I have noted[2] the occurrence of severe pain in the neck with other symptoms suggestive of diaphragmatic hernia in a patient in whom *x*-ray examination was more suggestive of eventration of the diaphragm than of diaphragmatic hernia. Neck pain was not observed as a symptom in seven instances of diaphragmatic hernia in my series, but in Hedblom's[3] Mayo Clinic series, there was pain referred to the left shoulder in 2 of 19 cases of diaphragmatic hernia. Neck pain is also of importance as a symptom of subdiaphragmatic abscess and was noted in my series in 2 of 4 cases proved by operation.

The distribution of pain and relation to meals suggest an involvement of the upper part of the alimentary tract. The radiation to the neck suggests implication of the diaphragm.

Notes on the Physical Examination.—The heart is in normal position. No special importance is to be attached to the systolic, rough murmur at the left, second, interchondral space, not transmitted to the neck. Under normal conditions, peristaltic sounds are present over the lower parts of the chest and may be heard over the left side as high as the third rib in front and the lower third of the scapula behind, and on the right side at a somewhat lower level. They are present in this case to a higher level in front than is normally to be expected. Though there is much variation in normal persons in their loudness and extent, their presence in front as high as the clavicle is suggestive of diaphragmatic hernia or eventration. Dulness and diminished breathing at the left base behind, without other signs, though common to a great variety of conditions, are consistent with encroachment from below due to diaphragmatic hernia or eventration. While the evidence up to this point is not sufficient to make a definite diagnosis of either of these two conditions, one or the other seems the most likely explanation of the symptoms and signs. Whether or not any importance should be attached to the history of diaphragmatic hernia in her sister I am unable to say. In my experience I have never known it to occur in two members of the same family.

Cardiac displacement may or may not be present with both hernia and eventration and does not help in the differentiation. The observation that the anterior costal margin moved equally and well on both sides and the bilateral presence of the diaphragm shadow is, however, of importance in the distinction. The diaphragm shadow is absent with eventration and its presence here speaks for hernia rather than eventration.

The bearing on the differential diagnosis of the normal respiratory motion of the anterior costal margins deserves further discussion. The diagnostic

[1] New England Jour. of Medicine, February 23, 1928.

[2] Arch. of Surg., January, 1927.

[3] Jour. Amer. Med. Assoc., September 26, 1925, vol. 85, pp. 947–953.

importance of the behavior during respiration of the anterior costal margins was emphasized by Hoover whose clinical and experimental studies indicate that the diaphragm acts in opposition to the intercostal muscles. The intercostals enlarge the transverse and anteroposterior diameters of the inferior thoracic aperture. Their action is opposed by contraction of the diaphragm

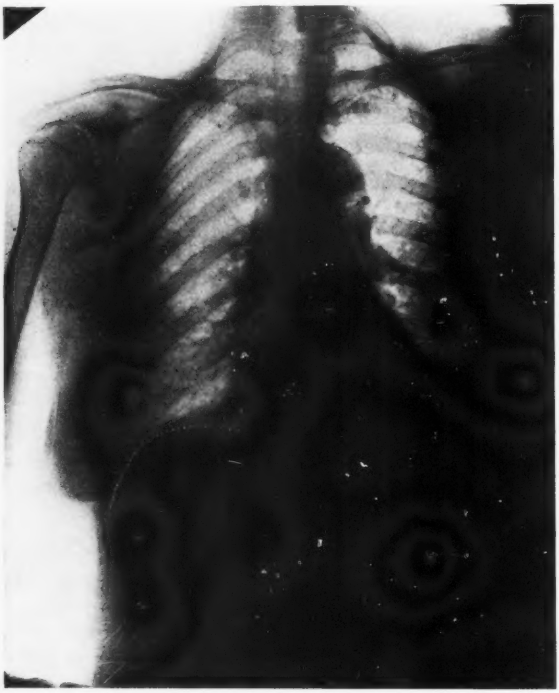

Fig. 1.—Diaphragmatic hernia. The outline of that part of the stomach above the diaphragm, behind the heart shadow, is shown by a dotted line. The fluid level of barium in this part of the stomach is also shown by a dotted line. The right leaflet of the diaphragm is shown. The left leaflet is not shown on this film. It could be made out on other films.

and the extent to which the diaphragm opposes the widening force of the intercostals depends on its arch. The more nearly the curve of the diaphragm approaches a plane the greater its mechanical advantage. Impairment of the action of the diaphragm by upward displacement as in eventration results in an accentuated upward pull of the intercostals and a greater widening of

the costal angle on the affected than on the unaffected side. I have observed an exaggeration of the inspiratory widening of the subcostal angle on the affected side in 2 cases of diaphragmatic eventration and its absence in this patient suggests that the antagonistic action of the diaphragm is not impaired and strengthens the supposition that hernia rather than eventration is the cause of the disturbance.

Results of Special Examinations.—The *x*-ray examination seems to establish the diagnosis of diaphragmatic hernia and there is from the *x*-ray

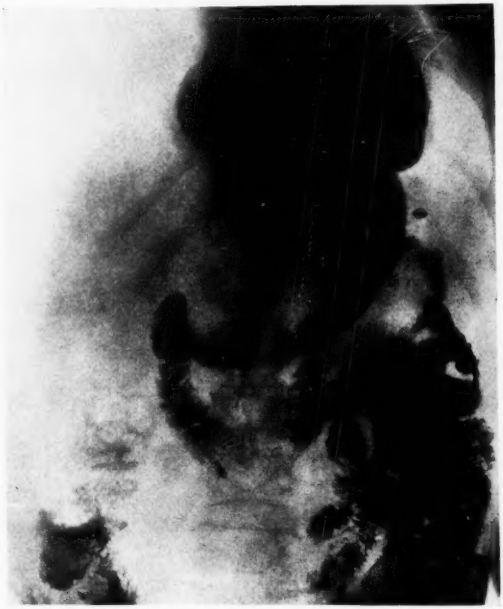

Fig. 2.—Diaphragmatic hernia. Roentgenogram after the ingestion of barium. That part of the stomach which is above the diaphragm appears as a cap-like shadow behind the heart. Below this is that part of the stomach which is below the diaphragm.

appearances no reason to believe that she has eventration of the diaphragm. In the film the right leaflet of the diaphragm can be seen and, in addition, a large mass of barium merging with the shadow of the heart. The bulk of the barium mass above the diaphragm is to the left of the middle line and continuous with a smaller mass below through a constricted area which may be regarded as the opening in the diaphragm.

The *x*-ray appearance with eventration of the diaphragm differs from

that observed here in the high position on one side, usually the left, of an unbroken arched line resembling the dome of an elevated diaphragm. Below this arched line the shadow of the gas-filled fundus of the stomach can usually be made out and external to this are likely to be shadows consistent with those due to the gas filled colon. Barium by mouth and by enema usually serves to identify the stomach and colon below the diaphragm.

The diagnosis of diaphragmatic hernia was seldom made during life before the use of the *x*-ray. It is still difficult to make the diagnosis without the assistance of an opaque meal. In the case under discussion the shadow of that part of the stomach above the diaphragm is obscured by the shadow of the heart and its outline has been traced with ink. The use of artificial pneumoperitoneum in the diagnosis of diaphragmatic hernia is usually unnec essary and subjects the patient to the risk of the production of artificial pneumothorax in consequence of absence of a hernial sac and imperfect closure of the defect in the diaphragm by the hernia.

Diagnosis.—The occurrence of epigastric and precordial pain closely related to the intake of food, and with radiation to the left supra- and infra-clavicular regions, the peristaltic sounds throughout the left front of the chest, and the dulness and diminished breathing at the left base suggested diaphragmatic hernia. The presence of the diaphragm shadow and the normal respiratory motion of the anterior costal margin served to make eventration of the diaphragm improbable. *x*-Ray examination established the diagnosis of hernia.

Outlook.—There is practically no prospect of relief without operation. There is considerable impairment of health and the risk that strangulation will occur with resulting gangrene and perforation. Operation was therefore advised.

Operation.—Exposure through a left upper rectus muscle-splitting incision showed, at operation by Dr. Daniel F. Jones, the upper third of the stomach in a large hernial sac above the diaphragm. The protrusion was at the esophageal opening, which admitted three fingers. The stomach was easily brought down into the abdomen. The peritoneum over the upper 3 inches of the stomach was thickened and callused. There was no evidence of pathology in the stomach or duodenum. The edges of the hernial ring were brought together with interrupted silk sutures, sufficient room being left for the esophagus only.

The gall-bladder was examined and found to contain several small stones about $\frac{1}{8}$ inch in diameter. A transverse incision was then made across the right rectus and the gall-bladder removed. There were adhesions between the gall-bladder and

the duodenum. The denuded area on the liver was covered with peritoneum. A rubber-dam wick was placed to the foramen of Winslow and the L-shaped wound closed about it. Convalescence was uneventful and Dr. Stockbridge reports, January 6, 1929, that the patient is completely relieved of symptoms and at work.

CLINIC OF DR. EDWIN A. LOCKE

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COMPLETE PNEUMOTHORAX OF UNKNOWN CAUSE ("SPONTANEOUS" OR "IDIOPATHIC" SO-CALLED)

THE case which we are to study today is of quite unusual interest because of its dramatic onset and exceptional display of signs not commonly met with in routine medical work. To the history of this case is appended brief summaries of three other examples of the same clinical condition which present several very important characteristics.

Case I. Complete Right Pneumothorax of Sudden Onset in a Young Athletic Man Without Obvious Cause.—A chauffeur of twenty-five entered the Boston City Hospital January 3, 1929 with the complaint of pain in the right chest and shortness of breath.

The family history is entirely irrelevant.

Past History.—Usually in robust health and apparently lives an entirely reasonable life. Weight about 138 pounds for many years. Drives a truck but work not laborious. Very moderate in the use of tobacco and alcoholic beverages. Whooping-cough, measles, chickenpox, and mumps as a child. Nine years ago gonorrhea but no complications. Six years ago and again last June severe attack of peritonsillar abscess. About a year ago he fell cutting the right side of his head badly and was treated in the Corey Hill Hospital. For many years he has been subject to severe migraine headaches, often occurring every day or two, but somewhat less severe and less frequent of late. Intermittent discharge from the left ear for some years but no history of acute disease of the ear at onset. No indigestion as a rule except some "gas," but bowels are very sluggish, as a rule moving only every two or three days. No history of any renal or cardiac symptoms. Moderate tendency to upper respiratory tract infections, and for two weeks prior to onset of present illness a very mild head cold with slight cough.

Present Illness.—Yesterday morning when getting into his truck after eating breakfast in a restaurant he was suddenly seized with a violent sharp pain all over the right chest. It was constant though not severe if he remained perfectly quiet in a sitting position in bed and on his left side. Any attempt

to take a full respiration, cough, sneeze or even move about greatly augmented the pain often causing him to cry out. At the beginning the pain radiated to the shoulder and was felt all over the right thorax back and front. When he entered the hospital, at the end of twenty four hours, the intensity of the pain had diminished considerably and it was largely confined to a rather limited area in the right front near the sternum. There was no tenderness over the painful area.

The initial pain was accompanied by very marked distress in breathing associated with a sensation of great pressure in the right front of the chest. Soon after the onset the patient felt intense nausea and vomited twice.

For about a half hour after the first symptoms developed he continued to handle his truck, but then was so overcome that he was taken home and went to bed. A doctor was called who gave him morphin and sent him to the hospital. During the past twenty-four hours the pain and dyspnea have gradually become less acute and the patient is quite comfortable so long as he remains quiet on his back.

Physical Examination.—Very robust young man, with high color, lying comfortably on his back on a bed rest. Although the face is deeply injected there is no cyanosis. Respiration shallow, 22.

The chest is well developed but slightly asymmetrical, the right being more prominent than the left. The intercostal spaces on the right are less well marked and the movement with respiration is almost nil. Litten's sign not made out on either side. The cardiac impulse is visible in the fifth space just outside the left nipple. Percussion over the left chest is possibly a little hyperresonant throughout, while over the right the note is a dull tympany. The limits of resonance on the right are greatly extended as compared with the normal, the usual area of liver dulness being almost completely obliterated. In the right back resonance extends nearly 3 inches lower than on the left and does not change with respiration. The apical outline is considerably increased on the same side. The right border of cardiac dulness is difficult to make out but appears to be at about the left border of the sternum while the left border is about 1 to 2 cm. to the left of the nipple-line. Respiration and fremitus over the left are of normal quality, though of moderately increased intensity while over the right chest they are very much diminished. Along the spine in back and the sternum in front on the right there is a moderately marked amphoric quality, and with both inspiration and expiration one hears a very loud whistling sound as though air were being forced through a small opening. With cough the amphoric tone is increased and in addition there is a very striking so-called metallic tinkle. The coin test is positive but no succussion can be obtained. No râles are heard. The examination is negative otherwise.

Sputum: Small amount mucoid material. No characteristic organisms found, no tubercle bacilli. Kahn negative. Urine normal. White blood count $\frac{1}{3}$ = 12,300; 1/10 = 9300; hg. 105.

The patient's course since his entrance to the hospital has been singularly even and although the recovery has not been rapid he has shown constant improvement. He was given absolute rest in bed for nearly four weeks in spite of the fact that he was practically free of all symptoms at the end of

the first week. Until recently deep breath or cough caused a feeling of distress or slight pain in the right chest. The temperature since the first few days has been normal. Successive *x*-rays have shown a very gradual expansion of the lung, apparently being complete at about the end of four weeks. He is the picture of health as you will see and no abnormal signs are at present to be made out in the chest.

Case II. Pneumothorax in Right Chest Followed by a Similar Lesion on the Left, and During the Course of Seven Years a Succession of Them, Making a Total of Eighteen Such Attacks. No Known Previous Disease of the Lungs or Other Cause of the Ruptures.—Man of twenty-four seen in consultation with Dr. Bernard Lederman, March 3, 1925.

Excellent general health and no illness of any sort until the present. Never subject to respiratory infections. He led an active athletic life.

About four years previously after a quiet day at home and while walking on the street he was suddenly seized with intense pain and sensation of great pressure in the right chest accompanied by intense dyspnea. On the previous day he had worked very strenuously lifting large packing cases but without any chest symptoms. The pain and distress were so great that he went to bed and was somewhat relieved by lying very quietly on his left side. Seen by Dr. H. Morrison who sent him at once to the Beth Israel Hospital.[1] The right chest is described as prominent, immobile, strongly tympanitic throughout, with greatly diminished respiration and fremitus. The heart was displaced moderately to the left. *x*-Ray examination showed complete collapse of the right lung with the mediastinal structures displaced to the left. Improvement was rapid and he left the hospital in one week. The temperature, pulse, and respiration were at all times normal. On the ninth day the record says there were no symptoms and *x*-ray indicated a considerable expansion of the lung. Satisfactory progress was made until the thirty-fifth day, when he had an attack exactly similar to the first, but with the symptoms in the left side of the chest and again while out walking. He was most comfortable lying on the right side. The signs were those of left pneumothorax with partial collapse of the left lung and slight displacement of the heart to the right. *x*-Ray examination confirmed these findings, showing a left pneumothorax with partial collapse of the lung and the heart moderately displaced to the right. No temperature developed and improvement took place gradually, the left being entirely normal at the end of two months. A second *x*-ray made at this time is reported as showing "marked infiltration at the right hilus, with increased peribronchial markings along both the left and right upper bronchial tree: both apices are clear."

During the next four years, or until seen on March 5, 1925, the patient had approximately fifteen attacks of the type described above but of varying severity as regards their duration. In some instances he was away from business only a few days, at other times the symptoms did not disappear for five

[1] The case was subsequently reported by Dr. Morrison (Boston Med. Surg. Jour., 185, p. 659, 1921) and the facts regarding his condition at this time are taken from his report.

or six weeks. With one exception the pneumothorax always occurred on the right. Except for the interruptions resulting from these attacks the patient led a normal and rather strenuous life and declares that he was perfectly free from all symptoms. His weight varied from 135 to 140 pounds.

When seen in consultation on March 5, 1925 he stated that he had had a severe attack of grippe three weeks previously and was just getting back to work when at about 4 P. M. on March 4, and while driving a car, he was suddenly seized with dull pain in the right upper chest and intense shortness of breath. When lying on his face these symptoms are almost entirely relieved, but if he turns on his back or stands up he has the sensation of a ton weight on the upper right chest and great dyspnea.

The patient is of rather spare type, but robust in appearance and fairly well nourished. He looks well and has excellent color. Nothing abnormal made out except in the thorax. It is difficult for the patient to remain long in any other than in a prone position on his face. The right chest is strikingly asymmetrical, the right being more prominent than the left and almost immobile during respiration. Over the entire right thorax the general percussion note is tympanitic and the limits of the lungs greatly increased, *i. e.*, the liver dulness almost obliterated, the apical outline more than twice as wide as on the left, and the lower limits in the back approximately 3 inches lower than on the other side. The right border of the heart is to the left of the sternum. The respiration throughout the same side is best described as faintly vesicular with a slight amphoric tone in the lower and outer part as is the vocal fremitus. With cough a distinct tinkle is heard but no râle or succussion. Temperature normal.

The recovery from this attack was remarkably prompt and in a few days the patient felt entirely well. On the fifth day after onset he was about as usual and free of all symptoms, but the signs of pneumothorax were still present. In spite of the absence of any definite evidence of pulmonary tuberculosis the possibility of such a focus as the cause of the repeated attacks of pneumothorax led us to advise him to undergo a course of treatment in a tuberculosis sanatorium. While a patient there for three months he had no respiratory symptoms whatsoever and no abnormal signs were found in the chest. The temperature remained normal. No sputum was ever available for examination. No tuberculin tests were made. The *x*-ray examination is reported as negative. Weight 140. Blood pressure 105160.

From this time (July 1, 1926) until March 10, 1927 the patient was at work regularly and free of all symptoms. On this date he suffered from a very severe attack. Dr. Lederman who saw him on this occasion found a complete right pneumothorax with the heart pushed far to the left. In five days the patient felt so well that he returned to work but at the end of a few days had a rather mild but typical attack on the left. Since this time he has remained well and free of all symptoms of pneumothorax. He has been examined frequently and always with negative results. Laboratory studies including the Wassermann test and *x*-rays have given no significant results. Vital capacity 3750 c.c., basal metabolism, 8 per cent.

About twenty years ago the patient's mother was sent to the Rutland State Sanatorium because of a persistent cough, where she remained for

about a year. There was never any abnormal temperature or tubercle bacilli found in the sputum. Since her discharge she has never shown any evidence whatsoever of tuberculosis and is now perfectly well.

Case III. Pneumothorax Left Chest Following Severe Exertion, Recurring from Similar Cause Eighteen Months Later. Questionable History of Tuberculosis. Recovery.—Lad of nineteen first seen September 16, 1913. The patient's mother considered to have had tuberculosis in her early years. The patient when nine months old was desperately ill for many months and a diagnosis of tuberculosis made. Operation at ages eight and eleven for cervical glands obviously tuberculous. Precarious health for many years through childhood but gradually improved in general condition until at age eighteen he was considered well. At this time however he was rejected as a candidate for West Point on the grounds of unsatisfactory physical condition, the examining board reporting "probable tuberculosis."

In spite of an almost certain history of tuberculosis a careful study in September, 1913 failed to prove the presence of the disease. An *x*-ray examination by Dr. A. George did not show changes in the chest characteristic of tuberculosis. The next four years were spent in Saranac Lake, Wyoming, New Hampshire, and Colorado "taking the cure." From August, 1917 to March, 1919 he served with the United States forces in Europe, for almost the entire time being in active service at the front and enduring incredible privations. Notwithstanding these hardships over a long period he was never so well in his life and reached his maximum weight of 172 pounds. After his discharge from the army a further careful examination did not show any evidence of tuberculosis. He was constantly under medical supervision for the next few years and improved constantly in general health.

On June 15, 1925 (thirty one years of age) while playing tennis he made a sudden and maximum effort and instantly felt a most intense burning pain through the left chest exactly over the heart radiating up to the tip of the left shoulder and after a few minutes down the whole left front of the chest. This was accompanied by intense distress for breath. He attempted to continue the game, but collapsed and was taken home. Observers described his condition as desperate. He was a slaty blue color and could merely gasp for breath. When he leaned forward he felt a desire to cough and had sharp pain just to the left of the sternum at the level of the fourth and fifth ribs. Cough, deep breath, or yawning induced very severe pain. He could lie only on the right side. Temperature 99.5° F.

The patient when seen twenty-four hours later seemed perfectly comfortable and looked well. He was lying on the right side on a high bed-rest and comparatively comfortable unless he moved about. The thorax appears symmetrical, though the left is immobile. There is definite tympany over the entire left chest. The left border of the heart is difficult to determine, but the right border is definitely in the right nipple-line. The respiration over the left chest both back and front is very distant, the voice muffled and indistinct. Tactile fremitus absent.

The patient appeared to have a slight cold following the accident and for a few days had a temperature of slightly over 99° F. After forty-eight

hours there were on symptoms except with exertion or coughing and by the end of two weeks felt so well that he went to the country. Examination of the chest seemed to indicate a considerable expansion of the left lung, but unfortunately an *x*-ray was not possible. On August 4th he reported for examination and nothing abnormal could be detected in the thorax. *x*-Ray plates showed the lung fully expanded.

From August, 1925 until December 6, 1926 he remained in excellent general health and continued his college work uninterruptedly. Except for two mild head colds there were no respiratory symptoms. On December 9, 1926 while doing very heavy work building a blast-furnace and when standing with the arms above his head straining to get some heavy pipes in place he suddenly felt an intense cutting pain in the left chest and great dyspnea. He was immediately taken home and put to bed where he was quite comfortable lying on the right side on a bed-rest. The patient's color was slightly dusky and the respirations thirty. With any moving about, the pain and dyspnea were much increased and sharp pain induced at the tip of the left clavicle. Physical examination showed signs of a complete pneumothorax as with the earlier attack but in addition very definite amphoric breathing and voice in region of the left hilus with marked metallic tinkling sounds brought out by cough. No succussion sounds or other evidence of fluid could be made out.

For some weeks following this occurrence there was a slight evening temperature and the patient remained in bed for a period of two months before the lung showed complete expansion. During the past two years he has been in excellent health and leading a very active life. Neither the examination of the chest nor the roentgenograms show anything abnormal in the chest.

Case IV. Pneumothorax Left Chest Without Known Antecedent Disease of the Chest or Other Obvious Cause. Recovery.—A school boy of eighteen seen in consultation with Dr. Sanford, Exeter, N. H., November 12, 1928.

The boy's mother has tuberculosis, but he has never had any evidence of the disease himself. Indeed, he has a remarkable history of good health and has felt especially well during this fall term in school. He is training with the track team, but has not run for several days nor has he done anything strenuous. Yesterday (Sunday) he was absolutely quiet all day sitting about his room studying for an examination. He had very slight head cold, but was feeling perfectly well. About 7 P. M. while sitting quietly in the cafeteria waiting for his dinner he was suddenly seized with a terribly sharp, boring pain localized in the region of the inferior angle of the left scapula, but very soon felt over the region of the pericardium and down the left arm. The pain in the front of the chest was not sharp as in the back, but described as if a ton weight were pressing him giving him pain and preventing respiration. He walked a short distance to his room, but seemed so ill that he was taken to the infirmary at once. His condition at this time was described as alarming. He was in a condition of shock, the extremities cold, the whole body moist, the facies livid, and considerable cyanosis. The respirations were very shallow, rapid, and possible only when in a sitting position on the right side. Lying on the back immediately increased the pain to an alarming degree and resting on the left side was quite impossible. The symptoms gradually

abated and after moderate doses of an opiate he was, in the course of two hours, able to get some sleep. In the morning he felt much relieved, although the pain was still present and he could lie on the back for only a few seconds. There was no longer any pain in the left arm.

When seen at 7 in the evening—twenty four hours after the onset—he was sitting propped up in bed and on the right side, breathing at a normal rate and apparently without dyspnea. Slight movement instantly induced both dyspnea and pain. His color was good, the skin was normal. Temperature 98.8° F.; pulse 76; respiration 20. The left thorax was distinctly more prominent than the right, and the interspaces less well marked. Respiration was very shallow but the right moved more than the left which moves not at all except as the whole thorax is lifted. There is no visible cardiac impulse. The right chest is normal to percussion while the left is hyperresonant throughout. There is complete dextrocardia, the right border being in the right nipple line, the left at about the right sternal border. The heart-action is a trifle labored but regular and the sounds are of good quality. Respiration and fremitus over the right side of the thorax are normal except perhaps slightly exaggerated. Both respiration and fremitus are absent on the left except near the midline. There is no metallic tinkle with cough and no succussion. Otherwise the physical examination was normal.

The initial improvement already described continued and within a few days the patient was entirely free of symptoms and the signs in the left chest had become almost normal. At the end of twelve days the chest signs were absolutely normal, *x*-ray showed the lung fully expanded and the heart in normal position. He was discharged from the infirmary to his home on the same day.

Pneumothorax in a great majority of cases occurs as a result, first, of some form of trauma causing a rupture of the lung or chest wall, and second, of some disease of the lung leading to rupture. Nearly all are of the latter group and occur with a considerable variety of primary diseases such as abscess, gangrene, new growth of the lungs, bronchiectasis, emphysema, tuberculosis, empyema, and pneumonia. By far the most common association is with pulmonary tuberculosis, although the pneumothorax is seldom complete in the sense of an entire collapse of the lung for the reason that pleural adhesions are almost always present to such a degree as to prevent complete retraction of the ruptured lung. This partial form of pneumothorax (the "small pneumothorax" of Barlow and Thompson) is relatively frequent in the course of pulmonary tuberculosis, but because of the limited collapse of the lung is not often recognized. In all these forms, at least a small amount and often a large

amount of serous or purulent fluid usually accumulates in the pleural cavity soon after the appearance of air.

In sharp contrast to this general group of pneumothoraxes we rarely see, as in the cases given you this morning, a complete pneumothorax developing in an individual who shows no evidence whatever of any intrathoracic disease. This type is usually designated as "idiopathic" or "spontaneous pneumothorax." Except for the absence of the evidence of any disease process leading to rupture of the lung this form does not present any unique features and I am inclined to regard the separation of these cases into a different group as entirely artificial. Furthermore, the term "spontaneous" obviously carries with it inferences as to the origin of the lesion which are entirely unjustified. Such a term as "unexplained pneumothorax" or "pneumothorax of unknown origin" seems to me much to be preferred.

Anyone seeking to acquire a thorough knowledge of pneumothorax should read the original description by Laennec written more than a hundred years ago. I have here a work entitled "A Treatise on Mediate Auscultation and on the Diseases of the Lungs" by Laennec in which is given a most complete and accurate description of pneumothorax. Indeed, the whole subject is treated so thoroughly that you will find little if anything essential regarding the condition in the modern text-books which is not to be found here.

As implied by the name spontaneous pneumothorax the condition is observed in individuals without evidence of any disease of the thorax. This is definitely true of all of the cases presented this morning with the possible exception of Case III in which there is a past history which is suggestive of pulmonary tuberculosis. A most careful study of the case over a period of many years, however, failed to prove the presence of tuberculosis and the evidence today is equally negative on this point. In Case II, likewise, there was a suspicion of the same underlying disease, but no evidence has ever come to light. The other 2 cases give a quite remarkable history of robust health without the slightest indication of any antecedent disease.

The very definition of this form of pneumothorax indicates that its etiology is unknown. Many theories have been advanced to explain the rupture of the lung. The most commonly accepted one is that rupture is the result of a tuberculous focus near the surface of the lung. One author expressed the opinion that in 90 per cent. of these cases air enters the pleural cavity as a result of perforation at the site of a tuberculous surface lesion. In a few instances cases are recorded in which tuberculosis subsequently did develop, but the number is so small as to carry no particular significance. We cannot then on the evidence accept the theory of an underlying tuberculosis in all of these cases. The almost uniform recovery in these cases gives no opportunity for postmortem examinations which would readily settle the point. The most natural inference is that the pneumothorax is due to a tear resulting from an adhesion of the lung to the chest wall. Such may well be the case in those individuals (Case III) whose pneumothorax immediately follows some very strenuous exertion or violent coughing or sneezing. Note that in Cases I, II, and IV there was no such factor present. All occurred when the victim was very quiet. How shall we explain the instances of recurring and complete pneumothorax? Case II has had a total of eighteen attacks in several of which careful examinations were made and the lung found completely collapsed. It seems clearly impossible that a new adhesion had formed each time. We may also think of the possibility of some weak point on the surface of the lung as a bleb which gives way, as has been suggested by several authors. The evidence, it seems to me, is all in favor of some such mechanical cause as the rupture of a vesicle rather than the presence of any actual disease. The most interesting thing and the most difficult to explain is the fact that rupture so often comes when the individual is in repose.

The pathologic anatomy in these cases depends on the degree of disease of the ruptured lung and adhesions of the individual structures if present. When the affected lung is not diseased the collapse is complete, the lung lying in the gutter of the spine as a small ropy mass, with no resemblance to the normal lung.

In all cases the heart is displaced more or less completely to the opposite side and to some degree the mediastinal structures also. The displacement of thoracic organs may be so great as to induce very distressing or even dangerous symptoms due to the compression of the well lung. When the pneumothorax is of large volume the diaphragm, liver, and spleen are displaced downward with marked encroachment on the other abdominal viscera.

Pneumothorax accompanying intrathoracic disease is usually complicated by a serous or purulent exudate, and often of large volume. In this type under discussion, however, fluid is almost invariably absent, at least in any appreciable amounts. It must be admitted that a small volume of fluid may be present without physical signs or evidence by *x*-rays.

The intrathoracic pressure becomes positive and has been recorded as high as +10 mm. of mercury. You will recall that the normal pressure in the pleural cavity is roughly −5 mm. during expiration and −10 mm. during inspiration (Stewart).

The vital capacity of the lungs in all forms of pneumothorax is diminished, the reduction being quite definitely proportional to the volume of air in the pleural cavity. The average vital capacity in a series reported by Myers was 51 per cent. below normal. The pleura itself shows no change unless infection takes place.

The symptoms are almost entirely dependent on the degree to which the respiration is embarrassed. When the condition develops rapidly and the volume of air in the pleural cavity is considerable the symptoms are numerous and severe. If, on the other hand, the condition develops gradually symptoms are not prominent and the condition may even be overlooked. It is indeed surprising how frequently even a considerable degree of pneumothorax may exist without pronounced symptoms of any kind and be found only on physical examination.

The above cases present a very typical clinical picture of the condition. The patient is seized with a very severe, often overwhelming pain, accompanied by intense dyspnea and feeling of suffocation. The pain is most apt to be felt in the upper midfront of the affected side or at the inferior angle of the scapula,

occasionally radiating to the shoulder and down the arm precisely as in the case of angina pectoris. After the first twelve to twenty-four hours the character of the pain changes to a dull pressure sensation as of a heavy weight on the chest. Cough or any attempt at deeper respiration often causes very sharp, lancinating pain through the affected side of the thorax. Occasionally in cases where the collapse of the lung is complete the symptoms are not urgent and the victim may keep about with the accustomed activities.

In the more severe cases the early symptoms described above are accompanied by tachycardia, deep cyanosis, and general symptoms of shock. Orthopnea is the rule in all except the mild cases. The valvular type of puncture sometimes gives rise to symptoms of extreme severity and may even lead to sudden death. Cough, though common in these cases, is seldom a prominent symptom. In the vast majority of cases all symptoms largely abate or entirely disappear at the end of a few days and the disease runs a slow but comfortable course.

Physical signs in pneumothorax while easy to describe are in actual practice sometimes quite indefinite and irregular. Laennec lays emphasis on this consideration and warns against the error of mistaking the well for the affected side. The cases presented today give an entirely unfortunate picture of the chest signs since they are all so uniformly typical.

During the acute stages inspection gives a very constant picture. The patient is sitting up in bed, breathing rapidly and with evident distress. Cyanosis is apt to be marked and if the dyspnea and pain are acute the entire body may be bathed in perspiration. The appearance of the chest may or may not be abnormal. If the pneumothorax is well developed the side involved is somewhat fuller than the other, the intercostal spaces being less marked, and the ribs immobile during respiration. In breathing the dyspnea is such as to bring the accessory muscles into play.

Percussion is usually stated to give signs which are extremely variable and often atypical, but this has not been my experience. The note all over the pneumothorax side in our cases was defi-

nitely hyperresonant (dull tympany), the percussion boundaries were enormously extended and did not change with respiration. It is clear that the character and intensity of the percussion note is considerably influenced by the character of the chest wall and the degree of tension. Displacement of the heart is readily demonstrated especially if to the right.

Auscultation tends to give greater variation in signs than does percussion. Most frequently the respiration is absent or extremely distant. When present it may be amphoric in type and at times intensely so. The vocal fremitus is of the same quality as the breath sounds and may even bring out the amphoric quality more clearly. A short cough will occasionally give an amphoric tone when not heard otherwise.

The most exquisite and interesting sound which is heard in a moderate percentage of cases is the metallic tinkle. It is most often heard in the presence of fluid as well as air in the pleura but is occasionally elicited when no evidence of fluid exists. The sound is hardly ever present without amphoric breathing and as in the case of the latter is often produced by cough. The coin sound is a nearly constant sign in pneumothorax and one of the most significant.

Death is of rare occurrence in spontaneous pneumothorax. The vast majority run a favorable course without severe symptoms after the first one or two days, complete expansion of the lung taking place in two weeks to several months, the duration apparently depending on the type of opening into the lung and the readiness with which it heals. A recurrence of the pneumothorax has been recorded many times as in Cases II and III. The former case is extraordinary, however, in the large number of attacks—eighteen during a period of seven years. A still more exceptional feature is the bilateral occurrence of the pneumothorax in this same case.

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ANEURYSM OF THE THORACIC AORTA; DIAGNOSIS; PULMONARY AND OTHER PHYSICAL SIGNS

THIRTY years ago the clinical diagnosis of aneurysm presented many difficulties and frequently was not made until the late physical signs appeared. These signs are increased transverse dulness in the aortic area, a thrill and diastolic shock often felt over the area; a loud second sound which, of course, may be absent if there is accompanying insufficiency of the aortic valve; a diastolic murmur may be heard if there is involvement of the valve; an aortic systolic murmur may also be present. Pressure symptoms are likewise late manifestations which produce a variety of physical signs such as interference with the superior vena cava causing engorgement of the vessels of the chest and arms; inequality of the radial pulses and pupils; a peculiar "brassy" cough which is characteristic; sometimes dysphagia and tracheal tug. In time a large tumor, often expansile, projecting from the chest wall may result from erosion of the sternum or costal cartilages. Pressure symptoms often cause agonizing pain which wears the patient out while on the other hand erosion may be painless. Erosion of the vertebral bodies commonly gives rise to boring, continuous pains. Many of the physical signs may be missing; the picture is rarely complete. A study of the protocols shows how variable the symptoms may be. Naturally the part of the aorta involved and the size of the tumor govern the symptomatology and the character of the pressure signs in neighboring organs. Chronic or recurrent pain in the chest is a very variable symptom of aortic aneurysm. In some patients a large aneurysm may erode cartilages and

appear at the surface of the chest without having made itself felt. In others agonizing pain may occur before an aneurysm at the root of the aorta has grown large enough to produce any of the above signs. Recurrent pain may suggest aortitis or occlusion of the coronary orifices and indeed may be due to both causes plus the aneurysmal pain since the same causative agent produced all these conditions. Pressure on the lung may easily produce pulmonary symptoms as seen in some of our cases and the pain may simulate a pleuritis. In one of my earliest consultations I mistook a pain in the usual area of a pleuritis for the pain of pleurisy and later was chagrined to find that I had overlooked an aortic aneurysm.

It may be difficult to decide between aortic aneurysm and mediastinal new growth. Here our greatest aid comes in the use of the *x*-ray, the rays being passed through the patient's thorax in a number of horizontal directions successively will establish the connection of the tumor with the aorta. Anginal pains and the severe pain of erosion are commoner in aneurysm than in mediastinal tumor.

Remembering then how variable the physical signs are, let us take a hypothetical case. A man between forty and fifty consults you because he tires more easily than he did formerly and when he exerts himself he notices that there is undue shortness of breath. At times there is pain in the chest with exertion, but if he is quiet he is quite comfortable. He frankly states that he had syphilis fifteen years ago or he may say that he never had any venereal disease. The examination of the heart by percussion and fluoroscope does not reveal very much; in fact the heart's sounds and size do not seem to offer a cause for apparent insufficiency. Percussion may show a slightly widened arch. Examine the terminal vessels carefully; atheroma may not be evident, but do not forget the retinal vessels—it may show there. The blood-pressure may or may not be helpful. Do a Wassermann and possibly a Kahn test, no matter what he says about his venereal history, remembering that syphilis is the greatest etiologic factor in aneurysm. It is not likely that any of the physical signs enumerated above will be present in a

very early case, but it is well to thoroughly investigate each of them. It is wise to have an *x*-ray in a variety of horizontal positions. That may also throw light on some puzzling pulmonary findings. That the heart can be essentially normal in the presence of a large aneurysm is well illustrated by Case II.

An aneurysm is a chronic dilatation of the lumen of an artery with new formation of the wall and thus is different from a mere dilatation because of the stretching of an atrophic wall or from an intra- or extra-mural hematoma. Most writers are of the opinion that syphilis is the common cause of aneurysm. Anders lays stress on the position of the aneurysm in distinguishing its etiologic variety, claiming that the ascending portion of the aorta is the usual seat of luetic aneurysms. The greatest number occur in the ascending portion and the smallest in the descending.

Various observers have reported 60, 80, 82, 85, and 95 per cent. due to lues. Anders in 621 cases found 58.5 per cent. of luetic origin, but considered the percentage was too low, since some of the cases had not had the Wassermann test.

Allbutt considered syphilis to be the common cause of aneurysm, and Osler placed the percentage as high as 80 or 85, and stated that nowadays it is rare not to find a positive Wassermann reaction in an aneurysmal patient under fifty. Osler believed that the specific fevers cause areas of degeneration in the aorta not uncommonly, but fortunately, in most instances, they are confined to the intima, but occasionally, as in typhoid fever, may cause changes in the media. He believed that infections other than syphilis play a minor rôle in the causation of aneurysm. Mallory says that tuberculous lesions of the arteries and aorta have in rare instances caused weakening of the wall and aneurysmal formation. Tuberculous lesions are very common in the capillaries and lead to complete occlusion of them. They occur more or less frequently in the small veins and arteries, especially in certain parts of the body, such as the lungs, for instance, and are dangerous because the tubercle bacilli may multiply in great numbers, and by escaping into the circulation give rise to acute generalized miliary tuberculosis. Rarely they lead to the forma-

tion of an aneurysm in arteries or the aorta, from which again large numbers of bacilli may be discharged into the blood (Principles of Pathologic Histology, 1914). Another point which I wish to call to your attention is emphasized by Harlow Brooks in an article on the heart in syphilis. He believes that it is unsafe to attempt to divide syphilis into periods or stages, since one commonly finds so-called tertiary lesions appearing in secondary stages, and from time to time in the tertiary period sudden exacerbations of the process spring up which can only be compared to those which we are accustomed to ascribe to the secondary stage. Brooks also calls attention to the early appearance of syphilis of the aorta in patients who have been thoroughly treated at the time of their initial lesion. It has been my experience with the majority of cases of syphilis of the aorta that the condition appears ten to fifteen years after the original infection.

Since this lecture is on some of the misleading chest signs of aortic aneurysm, I am going to recall a case seen several years ago. It was one of aneurysm of the descending aorta, the early diagnosis of which is so difficult and for that reason often overlooked. Osler said that it is frequently latent and that pulmonary and pleural symptoms are common. Pain in the back is the commonest symptom and is generally severe; dysphagia is not infrequent. This type of aneurysm may reach an enormous size. The following case illustrates the manner in which pulmonary symptoms may mislead us.

Case I.—The case is a white man sixty-three years old. He came into the hospital in 1908 with a fractured femur. At that time he had tortuous and thickened vessels and a systolic murmur at the aortic area. He was admitted again to the medical side of the hospital on June 12, 1919, from the Boston Consumptives Hospital where he had been for one year and four months. His family history was unimportant. His wife died at thirty-seven in childbirth and his only child died at the same time. The chief complaint was pain in the right hip and left chest existing for two years. He was unable to recall any diseases of childhood or adult life and was never sick in bed until he went to the Consumptives' Hospital. There was no history of precordial pain, vertigo, hemoptysis, chills, night-sweats, or edema. At times he felt feverish and for a year had malaise and pain in the left side. The night urine exceeded the day. The appetite had been fair and until one

year ago the bowels regular. He denied having any venereal infection. His habits were good. He smoked moderately and did not use alcohol. He had always done heavy work. Best weight 225 pounds eight to ten years ago, 175 pounds one year ago, and 170 pounds now. Two years before admission, while lifting a heavy casting in the Navy Yard, he felt a sudden strain in the right lumbar region. He was strapped by the yard doctor and continued work. The pain was persistent, but never interfered with sleep. At the time of admission to the Consumptives' Hospital there was slight cough, with morning sputum, and the patient was placed in a cottage ward for the slightly incapacitated. There were no signs of active tuberculosis for one year before admission to the Boston City Hospital, but three months before he had severe pain in the left hypochondrium. The pain was without relation to meals, did not radiate, and was not increased by breathing. He complained of general weakness, pain in the left hypochondrium (three months' duration), poor appetite, and constipation.

The general examination showed a well-developed, somewhat emaciated man lying comfortably in bed, without apparent distress. He answered questions readily and intelligently.

The head examination was essentially negative, while the expansion of the chest was good.

The lungs were dull throughout except in the left base, where the note was flat. Tactile fremitus and voice sounds diminished, but absent at the left base. Over the entire left chest, front and back, there were medium and coarse crepitant râles. In the right apex there were a few crepitant râles after coughing.

The heart was enlarged, 3.5 cm. to the right of the midsternal line and 13 cm. to the left. The cardiac impulse was seen and heard best in the fourth space just outside the nipple-line. The sounds were strong, with an occasional dropped beat. At the aortic area the second sound was accentuated. No murmurs. The vessel walls were slightly thickened and beaded. The brachials were tortuous. The abdomen was slightly rounded and tympanitic; no masses or tenderness except in the epigastrium. The liver and spleen were not palpable. The neurologic examination was negative. The extremities merely showed the results of old injuries.

While the patient was at the Consumptives' Hospital an *x*-ray plate of the chest was taken which showed a large shadow apparently connected with the heart.

The *x*-ray plate taken June 20, 1919 at the City Hospital (oblique view) showed a greatly enlarged transverse and descending aorta. The posterior mediastinum appeared to be clear. There was a large shadow in the left lower chest which was difficult of interpretation. The *x*-ray department suggested aneurysm of the thoracic aorta, and growth, either from liver or from some organ in the chest. The physical signs remained practically unchanged. The percussion note was almost flat over the left lower lobe behind. The left axilla, however, had normal resonance, so that fluid might be ruled out. There were many fine râles over this area and the breath sounds were markedly diminished. Fremitus was diminished and there was no Grocco's sign. The patient had lost a great deal of weight, as was manifested

by the flabbiness of his legs. There was a more noticeable and distinct shaking or shock of the patient's whole body with each heart-beat. The shock seemed to be entirely out of proportion to the heart impulse, which was barely felt in the fourth space just outside the nipple-line. The liver edge could be distinctly felt 4 cm. below the costal margin in the nipple-line. No pulsation could be felt in the abdomen even when the fingers were pressed deeply into the epigastrium. There was no evidence of an aneurysm in either groins or popliteal spaces. Patient had begun to be slightly dyspneic. He complained of pain only in his right hypochondrium, and he explained that this was due to a kick in the ribs which he received from a horse two years before.

Bismuth series was done on the patient to show the relation of the esophagus to the tumor. Anterior plates showed the esophagus crossing the chest from right to left and entering the cardia of the stomach in the extreme left side of the body. An oblique plate showed the esophagus pushed anteriorly by a big rounded mass. The interpretation of the *x*-ray and clinical findings was difficult. The mass might be either below or above the diaphragm. There was no question that the transverse and descending aorta were markedly enlarged. With this positive factor it seemed likely that the diagnosis of aneurysm of the thoracic aorta was the correct one. The patient's blood and urine were essentially negative. Wassermann negative. Patient failed rapidly and was markedly cyanosed. Had not developed hoarseness.

I will not give the complete autopsy findings, but only those relating to the aorta. It was greatly dilated in the descending portion, forming a large tumor mass, which measured 25 x 23 x 13 cm. This tumor mass, including the aorta, as well as the esophagus and stomach, weighed 3500 gm. Its outer surface was tough, firm, and blood stained and had attached to it by fibrous adhesions the esophagus, stomach, diaphragm, and a portion of lung. The esophagus entered the tumor at the superior border; and the cardiac end of the stomach was found at the inferior border. On opening the esophagus it was traced along the anterior surface of the tumor mass, making a half spinal curve. The mucosa was grayish in color, showing no signs of hemorrhage. It measured 5 cm. in thickness on the right and 8 cm. on the left, which was quite firm, dark gray in color, and showing well-marked laminations. There were areas which were reddish in color and more friable. The lumen through the mass varied from 4 to 5 cm. in diameter. The intima was smooth and dark red in color. Running vertically within the intima were threads of grayish tissue. Attached to the intima in places were soft dark red, jelly-like postmortem clots. The ascending aorta was dilated. The intima contained yellowish raised areas which more or less pinched it, producing a wrinkled appearance. This thickening of the intima was found throughout the aorta. The descending aorta from the arch to the tumor mass was gradually dilated, giving it the shape and volume of about a 500-c.c. Erlenmeyer flask. The tumor mass extended to 8 cm. of the iliac arteries. The circumference of the aorta here was 6 cm. The intima showed yellowish plaques. The arteries leading off from the aorta were dilated.

Case II. **Ruptured Aortic Aneurysm Complicated by Advanced Pulmonary Tuberculosis.**—J. F., forty-five years old, single, male, Jamaica negro employed as a stationary fireman, was admitted to the Second Medical Service of the Boston City Hospital, February 10, 1927. Four weeks before entry, while the patient was at his work, he was suddenly seized with a sharp, knife-like pain under the right nipple radiating to the right shoulder and later to the left chest and requiring him to give up his work. The pain continued with varying intensity, was not aggravated by deep inspiration, but was increased with cough or motion. He had mild "chills and fever," dyspnea on slight exertion, vomited twice, had a mild non-productive cough, and felt very weak and tired since the onset. He was unable to lie on his right side during this period because of pain. His local doctor advised him to enter the hospital suspecting an injury to the back. He was thus admitted on the surgical side on February 7, 1927. Here the patient showed no evidence of injury, but he was running a temperature of 100° to 102° F. and had a moderate cough. Pulmonary tuberculosis or other respiratory infection was suspected and an *x*-ray of the chest was taken which showed a mediastinal tumor. A medical consultant found no evidence of aneurysm on physical examination, but advised transfer.

The family history was essentially negative. In the past he had had several attacks of "fever" lasting two days each while in Jamaica and Central America. He had had eczema since childhood, and gonorrhea at sixteen, but denied syphilis by name and symptoms and said that he had been in good health until one year previous to admission. At that time he had an attack similar to the one which brought him to the hospital, but it lasted only a short while. He had anorexia, occasional headaches, and some loss of vision since then, and in the last three months preceding his present attack he had increasing dyspnea on exertion and lost about 30 pounds. He also had nocturia (two or three times a night). He gave no history of dysphagia, smothering sensations, hemoptysis, night-sweats, or edema.

On physical examination he was fairly well developed but poorly nourished and when first seen by us was in no apparent discomfort. His pupils were equal, regular, and reacted to light. He had marked pyorrhea, a coated tongue, and foul breath. There were a few small glands palpable in the neck. There was moderate dulness at the right top with harsh cavernous breath sounds under the right clavicle and a few crepitant râles elicited on cough over this area. The heart was not enlarged, the sounds were regular, of good quality, and no murmurs were heard. The rest of the physical examination was essentially negative. The temperature was 101° F., the pulse 100, and respirations 28. The blood pressure was 168–104, hemoglobin 80, white blood count 4900. The blood Kahn was negative. The urine was negative. No tubercle bacilli were found in the sputum.

There was no evidence on physical examination of aneurysm and the entire picture was more suggestive of pulmonary tuberculosis. The patient was apparently comfortable and not coughing much but was running a temperature of 101° F. On the evening of December 12th he had a violent coughing spell followed immediately by a profuse pulmonary hemorrhage. He tried to sit up, but had a convulsive seizure and fell back. His lungs filled

with blood, each inspiration became shorter and more difficult. Morphia was given immediately, but within fifteen minutes the patient had bled over a liter and died. In the laying out of the body, when he was turned on his face, a large amount of blood drained from his mouth and trachea.

The clinical diagnosis was pulmonary tuberculosis with pulmonary hemorrhage.

Necropsy performed by Dr. H. E. MacMahon revealed the following pathology in the chest: The right pleural cavity was completely obliterated by dense fibrous adhesions. The left contained about 200 c.c. of yellow cloudy fluid with flecks of fibrin. The pleura on both sides was yellow, opaque, and greatly thickened. The visceral surface of the left lung was covered with a greenish fibrinous exudate.

The heart was normal in size, shape, and position. It weighed 285 gm. The epicardium was thick, its anterior surface forming white, irregular, opaque patches. The myocardium, endocardium, and valves were negative.

The surface of the right lung was rough. Its apex was scarred and firm. Posteriorly in the dependent portion of the apex there was a large irregular cavity with no well-formed wall. The lung was red, tense, but not consolidated. The fresh surface was glistening, maroon, and dripped blood. The bronchi were filled with blood. None of the large bronchioles led directly to the cavity. The apex was studded with white glistening bodies resembling millet seeds. The left lung resembled the right in all respects except that there was no cavity.

The wall of the aorta had many yellow elevated plaques, a number of which showed parallel longitudinal striations. It was very elastic and showed no calcification. There was a well-formed saccular aneurysm of the transverse arch with extension backward and erosion of the bodies of the second, third, and fourth thoracic vertebræ. The orifice was round and smooth, 3 cm. in diameter. It had pushed the trachea and esophagus laterally without invading either. Lying along the anterior and lateral surface of the bodies of the vertebræ, it was very adherent to the lungs on both sides. On the right side it had embedded itself in the substance of the lung in a remarkable manner with complete disappearance of the pleura in this area. The wall of the aneurysm was thin and friable. Internally it had a rough, ragged, soft surface composed of blood-clot, and for a distance of 2 cm. from the orifice was lined by a yellow, smooth, glistening surface resembling that seen in the aorta. The stomach, duodenum, and upper third of the jejunum were filled with coffee-ground mucoid fluid.

The anatomic diagnosis was:

1. Rupture of a saccular aneurysm of the transverse arch of the aorta with extension posteriorly into the bodies of the vertebræ.
2. Pulmonary tuberculosis.

Case III. Aortic Aneurysm Simulating Pulmonary Tuberculosis.—F. S., a fifty-one-year-old white, single, American laundry man, was admitted to the Second Medical Service of the Boston City Hospital on October 21, 1928, complaining of "hemorrhage from the lungs and asthma." He had been working hard all summer up in Vermont and became "run down" and weak.

Four weeks previous to his entry he had caught cold which settled in his chest and failed to clear up. Since then he has had a moderate cough productive of a small amount of purulent sputum. Two weeks after the onset he had two asthmatic attacks on two successive days, both being relieved in a few minutes by adrenalin administered hypodermically by his local physician. Since that time he had some dyspnea on exertion and at night was uncomfortable unless propped up high on pillows but this has been steadily improving. Two days before admission, following a moderate coughing spell, he raised half a cup full of blood containing clots. Early in the morning of his entry, after an "argument" he raised, again after coughing, a large amount of blood and this was repeated four hours later. He thinks he raised about a pint in all. On entry he raised three clots the size of walnuts while the admitting physician was questioning him. In the past two months his appetite was poor, he had marked weakness, and lost 5 pounds in weight. He had never had night-sweats, fever, or chest pain, nor had he had any hemoptysis previous to those mentioned.

His family history was essentially negative and his only possible exposure to tuberculosis was his employment for six months in the laundry of a tuberculosis sanatorium.

He had had frequent attacks of "bronchitis" in the past few years; a urethritis in his youth. He denied syphilis emphatically on entry but later admitted having had a chancre at the age of twenty-six for which he received mercurials orally. His past history was otherwise negative and he was always in good health.

On physical examination, the patient was fairly well developed and nourished, he was propped up in bed in no apparent distress. His pupils were equal and regular and reacted to light. His heart was apparently not enlarged, the apex impulse being seen and felt in the fifth interspace 9 cm. to the left of the midsternal line. The rhythm was regular, the sounds of good quality, and no murmurs were heard. Because of the history of hemorrhage suggesting hemoptysis, percussion of the chest was omitted. The chest was somewhat fuller on the left with distended venules under the left clavicle. The neck veins were prominent, but equally so. No pulsations were observed in the upper chest. The breath sounds were somewhat diminished. There were many inspiratory and expiratory musical râles and a few crepitant râles at both tops. Over the right scapula the breath sounds were very high pitched and prolonged, suggesting amphoric breathing. The left arm was obviously larger than the right (the patient was left handed), but the pulses were equal and the veins apparently the same in both arms. The rest of the physical examination was negative.

The blood hemoglobin was 85 (T), red blood-cells 4,270,000, white blood-cells 7300, of which 68 per cent. were polymorphonuclears, 24 per cent. lymphocytes, 6 per cent. large mononuclears, and 2 per cent. eosinophils. The blood smear was negative. The non-protein nitrogen was 0.42 per cent. The blood Wassermann was negative and the Kahn positive. No tubercle bacilli were demonstrated in the sputum. The urine showed a slight trace of albumin and a few hyaline and fine granular casts.

A tentative diagnosis of pulmonary tuberculosis was made and the

patient treated accordingly. *x*-Rays taken three days later were interpreted by Dr. Paul Butler as follows: "Films show a tumor mass in the upper mid-chest, circular in outline, about 3 inches in diameter, probably aneurysm on the left side of the arch of the aorta. Study of the esophagus shows it displaced to the right, compressed, and in close proximity to the tumor mass."

The patient was apparently comfortable until early in the morning of the 25th when he suddenly had a huge hemorrhage, raising about 1 quart containing large clots, and expired soon after. The final diagnosis was aneurysm of the descending arch of the aorta rupturing into the esophagus, and pulmonary tuberculosis with cavitation of the right apex.

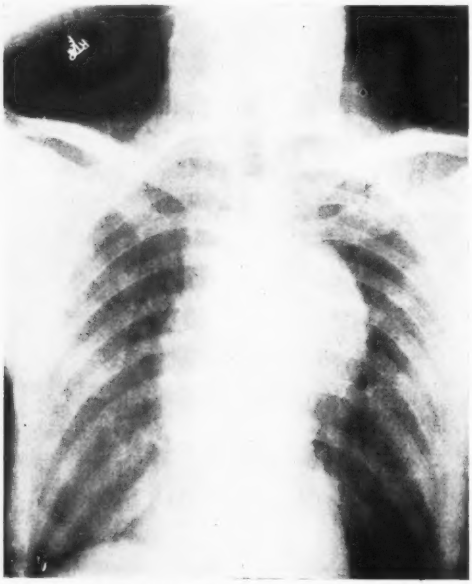

Fig. 3.—Case III. Esophagus; anteroposterior.

Autopsy was performed by Dr. A. G. Rewbridge and showed a few bands of fibrous adhesions joining the viscera and parietal surfaces of the left apex. The heart weighed 380 gm. and was entirely negative. The surface of the aorta near the aortic valves was studded with irregular flat yellow areas about 0.5 cm. in diameter. The arch of the aorta was somewhat dilated. There was a great roughening in the lining which was thrown up into irregular folds and nodular swellings, some translucent and pearly, others yellowish and opaque. At the left extremity of the arch and occupying most of the thoracic arch was a round saccular aneurysm which projected from the posterior and left aspect of the vessel. The opening leading

to this sac was round and measured 3 cm. in diameter. The aneurysm was adherent to and eroded the left aspects of the bodies of the vertebræ. A moderate amount of antemortem clot covered the posterior surface. Near the neck on the right side of the sac is a small opening which communicated with a similar opening in the esophagus at which point the aneurysm had ruptured. There was no evidence of communication between the aneurysm and the trachea and bronchi. The lungs were entirely negative. In the stomach a postmortem blood-clot formed a mold of the gastric interior. There was blood in the small intestine, and the feces in the colon were tarry. The rest of the autopsy was negative.

The anatomic diagnosis was aneurysm of the descending aorta ruptured into the esophagus; syphilitic aortitis.

Case IV. Ruptured Aortic Aneurysm Simulating Coronary Occlusion.—This case is of interest from its pathologic as well as its clinical aspect; the latter can be somewhat better appreciated when the facts are presented.

C. M., a fifty-one-year-old, single, male, Irish porter, was brought to the Boston City Hospital from his place of employment in a prominent down-town store on the evening of December 3, 1928 and was admitted to the Second Medical Service. When first seen by the house staff the patient's general appearance was that of extreme pain and shock. He was lying on his right side, doubled up in jack-knife position and was reluctant to do anything requiring the least effort, even to speak. The history obtained at that time was, therefore, very brief and the examination done without moving the patient in the least.

On the day of admission just before the closing time of his store the patient was going about his work as usual when he felt a desire to cough, but as he was about to do so he was suddenly seized with an excruciating pain beginning over the left scapula, radiating down the left axillary region and around the left costal margin to a point under the sternum, just above the xyphoid, where it remained more or less localized and vise-like in character. The pain was so severe that he was unable to remain on his feet and he dropped to the floor, but did not, however, lose consciousness. A few minutes later the patient vomited some yellowish material containing no blood. He was very slightly relieved by this. The store physician was called and, after administering some hypodermic medication, sent the patient to the hospital. The pain was still present, though somewhat less marked, when the patient was first seen, and he felt entirely exhausted.

For three or four weeks previously he had had moderate, sharp recurrent pains radiating from the left scapular region around the costal margin to the sternum. These were not severe enough to interfere with his work. He had had no recent cough, dyspnea, palpitation, or edema. He said that two years previously he was brought to this hospital for a similar attack and remained here for six weeks.

The patient was a fairly well-developed but rather thin individual lying motionless in the position described above, apparently in pain. He was very pale and his skin cold. His respirations were rather shallow, their rate 24 per minute. There was no evident cyanosis. The scleræ were clear, the

pupils were slightly contracted but were equal and regular and reacted to light. The cardiac impulse was rather diffuse, but the heart was not apparently enlarged, the sounds were weak, the first sound at the apex and base being roughtened, and a soft systolic murmur was heard over these areas. The rhythm was regular. The chest was the long thin type. The respiratory murmurs were barely audible. A few crepitant râles were heard at the bases. The radials, brachials, and temporals were hard and tortuous. The pulse was of poor quality, rate 88. The abdomen was soft and no masses felt. The temperature was 97° F., the blood-pressure (in the left arm) was 98/70, the white blood-cells 12,700, hemoglobin 60 (T), red blood-cells 2,980,000.

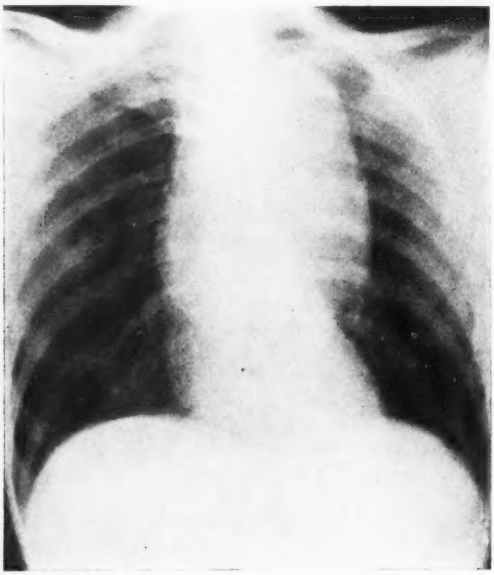

Fig. 4.—Case IV.

A tentative diagnosis of acute coronary occlusion was made. Morphia, gr. $\frac{1}{4}$ s. c., was given. The patient felt relieved after a short time and fell asleep.

The following morning the patient had no further pain and was apparently comfortable, lying flat on his back. In this position the following additional physical signs were made out:

1. The veins in the left side of the neck were markedly distended.
2. The venules over the upper part of the anterior chest were dilated.
3. There was moderate bulging of the upper left chest with a slight diffuse visible and palpable pulsation in the left infraclavicular fossa.

4. The supracardiac dulness was 10 cm., the increase being largely on the left.

5. The aortic second sound was loud and booming.

6. The carotid and radial pulses were appreciably more forcible on the right th anon the left.

7. Adefinite tracheal tug was demonstrated.

8. The blood-pressure in the right arm was 120/60; in the left was 100/70.

On the basis of these additional findings the diagnosis was made of aneurysm of the aortic arch with rupture or dissection to account for the phenomenon which brought the patient to us.

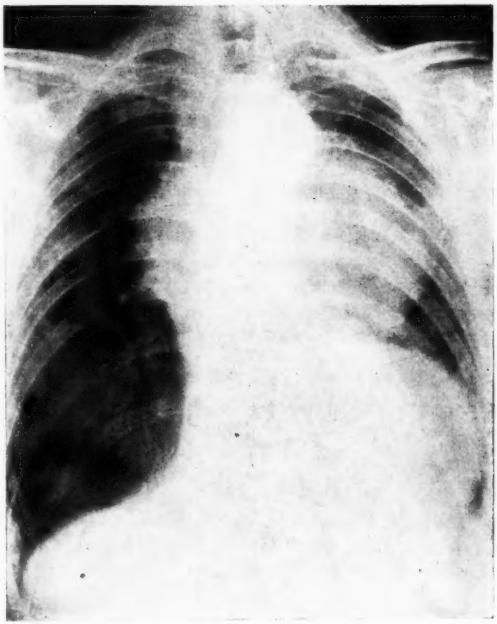

Fig. 5.—Case IV. Anteroposterior view.

The history of his previous entry was then obtained and it was found that the patient was admitted to the Third Medical Service on October 13, 1926 complaining of vomiting, diarrhea, and abdominal pain of four days' duration which had practically subsided on entry. His past history was negative except for recurrent winter coughs. He denied syphilis. On physical examination a widened supracardiac dulness was made out which corresponded to a non-pulsating mediastinal tumor seen under the fluoroscope. Dr. Butler's interpretation of the plates (one of them shown in Fig. 4) is as follows: "Films

show large tumor mass in upper central chest 5 inches wide by 7 inches high, more to the left than on the right side. Diagnosis: Either aneurysm or sarcoma. The continuity of the left border of the mass with the thoracic aorta probably indicates aneurysm." *x*-Ray examination of the gastro-intestinal tract was negative. The blood Wassermann was negative on three occasions, the Kahn was weakly positive on two. Because of the possibility of a mediastinal sarcoma, three *x*-rays treatments were given without change in the physical or *x*-ray signs and the patient was discharged November 15, 1926 with a diagnosis of gastro-enteritis? sarcoma of the mediastinum? aortic aneurysm? He was advised to return two weeks later for further *x*-ray studies but failed to appear until his present entry.

No further details of history could be obtained. The patient remained at absolute rest in bed and was apparently comfortable for about forty-eight hours. His temperature was normal, the pulse much improved as was his general appearance. On the evening of December 5th, when the nurse was coming toward him, the patient tried to sit up in his bed, requesting the nurse to rub his back. Before she could reach him he fell back, became cyanotic and had a generalized clonic convulsion. One of the house staff who was close by, saw the patient at this time. No heart sounds could be heard but the patient kept breathing about three or four times a minute. Intracardiac adrenalin, 8 minims of 1 : 1000 solution failed to start the heart and the patient expired shortly after this.

At postmortem, performed by Dr. A. H. MacKeen, the heart was found to be normal in size, shape, and position, there were several thickened white plaques upon the epicardial surface of the right ventricle. There was some thickening over the mitral valves and the aortic cusps were slightly deformed and showed sclerosis, at the bases of the latter there was some thickening with separation of the insertion of the cusps. There was moderate sclerosis and narrowing of the coronary orifices, the arteries themselves showing very little sclerosis. The right lung showed marked anthracosis and thickening of the bronchi but was otherwise negative. The left lung was compressed at the apex by aortic aneurysm and hemorrhage within the cavity. At the base the pleura was infiltrated with blood which had leaked from the aneurysm. The left pleural cavity contained 1500 c.c. of clotted blood, the right contained about 300 c.c. of hemorrhagic fluid.

The ascending, transverse, and thoracic aorta was extensively scarred and wrinkled on its internal surface. The scars were longitudinal and extended deeply into the wall. There was a slight amount of calcification along with the coexisting atheromatous plaques. The first portion of the ascending aorta was dilated to a diameter of 7 cm. This dilatation was present as far as the arch, but at the arch it narrowed down to 2 cm. in diameter and immediately afterward it was widely dilated again to a diameter of 8 cm. The latter dilatation was saccular and projected posteriorly and the sac was filled with blood-clot. The sac had ruptured posteriorly into the left pleural cavity and the blood had tracked down the soft tissues of the posterior mediastinum behind and around the esophagus and posterior wall of the stomach. The abdominal aorta showed atheromatous plaques with some calcification but there were no longitudinal scars. Posteriorly and laterally the aneurysmal

sac was pressing upon the fourth and fifth thoracic vertebræ, eroding them to a depth of 1 or 2 cm. On the posterior wall of the duodenum, about 1.3 cm. from the pyloric ring, there was a punched out ulcer 0.5 cm. in diameter, having thickened edges and base.

The right kidney measured 18 by 10 cm., was soft and cystic and contained a large stag-horn calculus and several smaller fragments. The kidney tissue was completely destroyed and there remained only a thin-walled sac divided slightly by the walls of the dilated calyces. The right ureter was patent, but its walls were thickened.

The anatomic diagnoses were: Aneurysm of aorta with rupture; erosion of vertebræ; hemothorax, chronic pyelonephrosis, and nephrolithiasis (cystic kidney); duodenal ulcer.

Case V. Large Aortic Aneurysm Without Pressure Symptoms.—The last case is interesting because it represents the oldest patient I have seen with aortic aneurysm. Syphilis is usually acquired in the earlier years but in this patient the infection must have come late in life or have been very slow in attacking the aorta. The history does not disclose the date of the primary lesion.

R. V., a seventy-six-year-old male, single American cook, entered the Second Medical Service of the Boston City Hospital September 24, 1928 complaining of difficulty in urination and a fainting spell. He had always been in good health until a few years before entry, when he began to have difficulty in starting his urinary stream. He had been undergoing treatment (prostatic massage and catheterization) in the out-patient genito-urinary clinic and after the visit preceding his entry had fainted on the street and was brought into the hospital. He had had some dyspnea on exertion noticeable on climbing stairs, but had never had any cough, precordial pain, edema of the ankles, or orthopnea. Nine years previously he had an "apoplectic stroke" with complete left hemiplegia from which he recovered almost completely but was left with residual numbness in the legs of "ascending nature," worse on the left. This persisted, though much improved, until the time of his entry. Seven years ago he was operated on for a chronic duodenal ulcer and a posterior gastro-enterostomy was done. The surgeon's operative notes mentioned a diffuse area of induration in the pylorus and first portion of the duodenum. He was thus relieved of abdominal pain, nausea, vomiting, and belching of which he had complained for several years previously. He had no recurrence of these symptoms. His blood was not examined at that time.

Physical examination on entry showed a well-developed and fairly well-nourished white man lying comfortably in bed without distress and breathing easily. His only complaint was weakness. He had slight urinary incontinence. The temporal vessels were tortuous and the radials and the brachials beaded and calcified. The neck veins were not distended. The heart was not enlarged; the apex impulse was not visible, but was palpable in the fifth space in the midclavicular line, the sounds were of fair quality and regular. The lungs were clear and resonant. The abdomen and extremities and reflexes were negative.

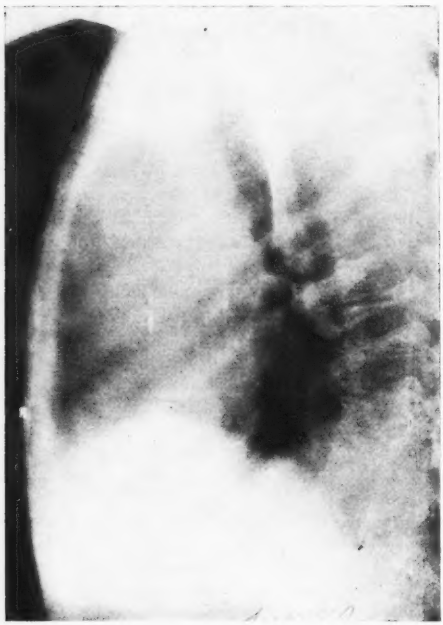

Fig. 6.—Case V. Lateral view.

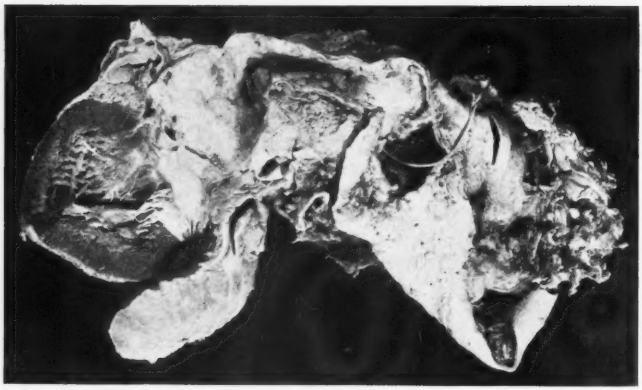

Fig. 7.—A case of aortic aneurysm simulating pulmonary tuberculosis aneurysm of descending portion of arch of the aorta; rupture.

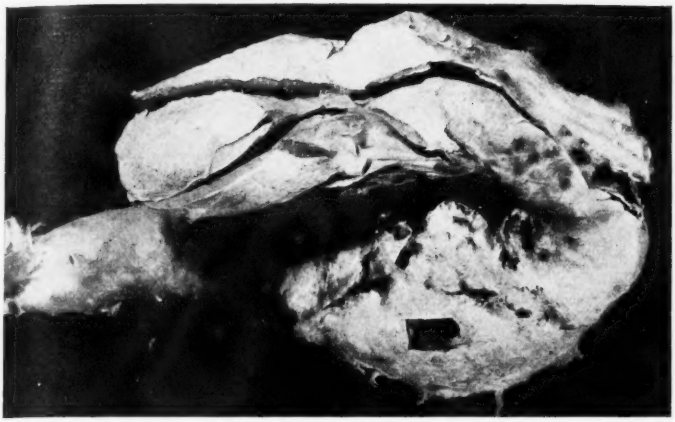

Fig. 8.—A case of ruptured aortic aneurysm simulating coronary occlusion. Aneurysms of ascending and descending portions of aorta.

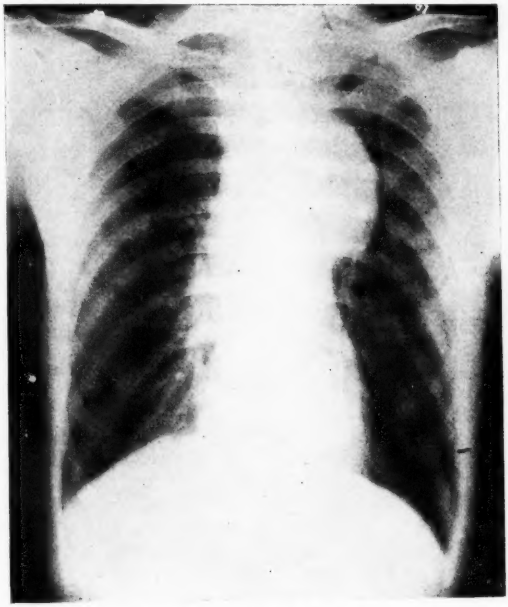

Fig. 9.—Case V. Chest.

With rest in bed the patient's clinical condition began to improve. The diagnosis was apparently generalized arteriosclerosis and benign hypertrophy of the prostate.

While still in bed on the wards awaiting his transfer to a chronic hospital the patient had blood-streaked sputum for the first time on November 13th. He raised small quantities for two days and then had a hemorrhage of about 1½ pints. At this time, on careful examination, a visible and palpable elevation and pulsation was made out in the second left interspace; and an aortic arch, widened to the left, was made out. An *x*-ray plate of the chest showed a large mediastinal mass, probably aneurysm. The plates were interpreted by Dr. Butler as follows: "The left diaphragm is elevated about 5 inches higher than normal. There is a large tumor mass about 6 inches wide and 5 inches high in the mid-chest region, larger on the left than on the right. The lateral view shows this tumor mass all anterior to the posterior mediastinum. The trachea is displaced slightly to the right by the mass. Diagnosis: Probably aneurysm confined to the anterior chest."

Even with this evidence, no signs of pressure could be made out. The pupils were equal, the arms apparently equal in dimension, the radial pulses were the same, the blood-pressure in the right arm was 110/82 and the left 108/88. There was no dyspnea, edema, venous or pulmonary congestion demonstrable. The Kahn on entry was negative (probably some error) but when repeated after the hemorrhage both Kahn and Wassermann were positive. There has been almost constant expectoration of blood-streaked sputum, though decreasing in amount and there is practically no cough now.

The patient is slowly failing in much the same manner as many of our cases of myocardial and circulatory degeneration. His previous cerebral accident was an indication of his general circulatory state and might easily have occurred in any circulatory breakdown.

The patient had a large hemorrhage followed immediately by death. No autopsy could be obtained.

My thanks are due to Dr. Maxwell Finland, resident physician on the second medical service, for assistance in preparing the protocols.

CLINIC OF DR. GEORGE P. REYNOLDS

FOURTH MEDICAL SERVICE, BOSTON CITY HOSPITAL

PHYSICAL ILLNESS AS AN ETIOLOGIC FACTOR IN PSYCHONEUROSIS

Introduction.—In the treatment of a case of psychoneurosis perhaps the most important factor is the explanation to the patient of the development of his symptoms from their original etiology. A recent analysis that I have made of 200 cases, which is to be published at a later date, shows that a very common cause of neurosis (42.5 per cent. of the series) is the impairment of a normal physiologic function of the body, in other words, a physical disability or illness. The following cases are presented in order to illustrate two ways in which a physical illness may upset the nervous equilibrium. In the first case the patient's anxiety over the purely physical aspect of his condition developed into a neurosis; in the second, an impairment of function in an organic system of the body so upset the physiology of the whole organism that the nervous system also functioned improperly.

Case I.—A married man of thirty-five years of age, a research worker in chemistry at a leading Canadian hospital, came to the hospital complaining of nervousness, insomnia, depression of spirits, and pain in the right lumbar region. He had been perfectly well until six months before entry, when he had had a mild, but typical, attack of renal colic, lasting only for one hour. It had occurred at night and he had not called a physician. The next day, however, while lunching with a group of medical friends, he described his symptoms and was given the probable diagnosis of "renal stone." The patient had the degree of "Ph.D." in chemistry, but had not taken a medical course, and so, having no clinical knowledge, was obliged to ask for more detailed information as to the nature of renal stone. He was considered to be a calm phlegmatic type of person, and had frequently expressed his contempt for individuals who objected to the pain and discomfort of such laboratory procedures as the taking of blood, gastric analysis, and the like. There-

fore his physician friends had no hesitation in telling him of the probability of a recurrence of his renal colic, the pain of cystoscopy, the discomfort subsequent to it, and the possibility that operation might eventually become necessary. They probably did not exaggerate the situation particularly, but there was certainly no attempt to minimize its unpleasant features.

The patient said little, but worried over this information a good deal. A fortnight later he had another mild attack, which he kept secret, and then, soon afterward, a third which was so severe that he was obliged to call in a genito-urinary surgeon. The surgeon, after a careful examination and urinalysis, agreed as to the probable diagnosis, and recommended cystoscopy. The patient, although frankly apprehensive, acquiesced and an appointment was made for a later date. During the intervening period, however, he became extremely nervous and irritable, and, when the appointed time arrived, he was hysterical and absolutely refused to submit to the procedure.

From that time until his entry into our hospital he had only one or two mild attacks suggestive of renal colic, but his nervous equilibrium was so completely upset that, though he continued with his work, he was never free from the dread of another attack, and the mere mention of cystoscopy filled him with an almost uncontrollable fear. His friends realized the situation and made every effort to reassure him, without the slightest success. He began to suffer from insomnia, his head ached constantly, and he developed a dull pain in the right lumbar region, which, though in all probability purely functional, only served to increase his phobias. Finally, he came to the realization that he was in a state of nervous exhaustion that was far more serious than the possibility of a renal stone, and was prevailed upon to seek medical advice in some other locality, and so came here.

It was not necessary, for the purposes of this discussion, to go into his subsequent history. Suffice it to say that a careful psychologic study failed to reveal any other cause for his neurosis, and that, with the proper rest and psychotherapy, he eventually recovered his mental equilibrium, although a renal stone was proved to exist in the pelvis of his right kidney. The point to emphasize, however, is that this man was a strong, rugged individual with no previous history of even a tendency toward nervous instability who developed a profound neurosis as the result of an organic lesion, and his dread of its consequences.

Case II.—The patient, a married woman of twenty-four years of age, came to the hospital complaining of fear of crowds, dizziness, palpitation, spasmodic rigidity of the neck, and weakness of the legs. All the symptoms were transient, but came in "attacks," usually when the attendant circumstances made them most inconvenient. For example, she frequently had palpitation and dizziness when she was "making a fourth" at bridge, but never when there was a fifth person available to take her place. She was much more liable to be seized with a feeling of oppression in the middle of an act at the theatre than at the "movies," where she felt that she could get up and go out at any time without being conspicuous.

She dated the onset of these symptoms from a mild emotional upset that occurred two years before at a funeral, which she had attended, as she

expressed it, "from a bored sense of duty rather than from any intimacy with the family," some of whom were distant relatives of her husband. Quite unexpectedly, in the midst of the ceremony she found that the grief of the chief mourners was affecting her own emotions; she felt faint and had to leave the church, but was perfectly well as soon as she got out-of-doors. She recalled that she was rather ashamed of herself for being so easily upset, and was embarrassed at the thought of how conspicuous she must have been. However, as she was three months pregnant at the time, and feeling miserable, she gave no serious thought to the faintness, which she attributed to her condition. It was not until some weeks after this episode that she began to have the nervous seizures of which she complained on entry. They were mild at first, and she paid little attention to them until after the birth of her child, when, despite her rapid physical improvement, the nervous symptoms not only persisted, but became more frequent and more severe. They continued to progress until she was unable to go shopping or to make definite engagements of any sort for fear of an attack. This state of affairs existed for months before her first visit to the hospital so that she had given up almost all her normal activities, and was in a state of profound nervous exhaustion.

She had had repeated negative physical examinations by competent physicians in whom she had perfect confidence, and was thoroughly convinced that her symptoms were purely neurotic. But she was not at all satisfied with the supposition that the incident at the funeral was the primary etiologic factor, because she was sure that she had been frequently, in the past, under a much greater emotional strain without any disturbance of her nervous equilibrium.

Her past history, from the psychologic point of view, revealed nothing of significance. There had been no previous evidence of a neurotic tendency, nor could there be elicited any emotional factor in her life which might be considered as cause for a neurosis. Her childhood and home surroundings had been excellent; she was happily married; the sexual relation was normal; and there were no financial difficulties. She had been perhaps a little overconscientious in her housekeeping and in the care of her three children, but she had led a very normal, healthy life, was of a cheerful disposition, and had an abundant fund of common sense.

One sister had had a definite, though mild, neurosis, but the remainder of her family history—including that of both parents and two brothers—was entirely negative.

A careful physical examination failed to reveal the slightest evidence of organic pathology. The routine examinations of urine and stool were negative, but a critical study of the blood brought to light the interesting fact that, although the hemoglobin was 75 per cent. and the red blood-cell count, 4,650,000 per cubic millimeter, the red blood-cells were classical of those found in mild chronic secondary anemia. There was a definitely abnormal variation in the size and shape of the cells, moderate achromia, a moderate number of microcytes and many elongated oval-ended cells.

Although it was difficult to conceive of more than a very remote connection between this slight anemia and the patient's nervous symptomatology, it was the only clue there was to go on, and so an attempt was made to deter-

mine the cause of the anemia and the date of its appearance. Careful questioning of the patient elicited the information that throughout each of her three pregnancies she had vomited several times a day, felt miserable, and was told that she appeared "anemic." A consultation with her obstetrician confirmed this, and added the definite knowledge that the anemia had become quite marked in the latter part of her third pregnancy, that is shortly before the neurosis developed, that there had been a considerable loss of blood when the child was delivered, but that the hemoglobin and red blood-cell count had rapidly returned to normal during the puerperium. However, as there had been no subsequent cause for blood deficiency, either from her diet, her physical condition, or from loss of blood, it seemed justifiable to assume that the existing anemia, as evidenced by the abnormal appearance of the cells, had persisted ever since her last pregnancy. Moreover, inasmuch as her nervous symptoms appeared shortly after the development of the anemia, the latter might be considered as playing some etiologic rôle in the production of the neurosis. In other words, no psychic cause for her symptomatology having been found, the hypothesis was adopted that it was simply an external manifestation of a lowered nervous resistance, which, in turn, was the result of the anemia.

The situation, at this point, was explained carefully to the patient, who was greatly pleased to think that an organic cause for her difficulties had been found. She was sent away from home to relieve her of her household cares, and instructed to partake of a nutritious, adequate, well-balanced diet rich in meat, fruits, and green vegetables, with approximately 180 gm. of cooked liver per day. In addition, she was given large amounts of iron by mouth (Blaud's pills, 3 gm. per diem) and generous doses of cod-liver oil. She was encouraged to take plenty of outdoor exercise but was asked to rest for two hours in the middle of the day in order to aid in relaxing the nervous tension.

At the end of a month of this régime there was a very marked improvement both in the blood-picture and in her functional symptomatology. The red blood-cells then varied but little in size and shape. Microcytes were absent and many fewer elongated oval-ended cells were present than formerly. The achromia had practically disappeared. Thus her red blood-cell picture had become practically normal. She reported that she was in excellent spirits and felt physically better than she had for years, but that she still tired rather easily. This circumstance was a natural one to expect after two years of marked nervous tension and slight anemia. When tired she had had a return of her symptoms, but she said that the attacks were much less severe and of shorter duration, and that she was always able to continue whatever she was doing, which had not been the case before treatment. Furthermore, she had dined out a great deal and had twice thoroughly enjoyed an evening at the "movies." The latter was particularly pleasing to her, because for nearly a year she had not been able to sit in a theatre more than a few minutes without experiencing a feeling of dizziness and oppression which usually became so severe that she was obliged to leave.

Altogether, the outlook was most encouraging; the anemia had been eliminated from the picture, and the nervous symptoms were rapidly dis-

appearing. The patient and her husband had been planning a yachting cruise and she felt perfectly confident that she would not only enjoy it, but that she would be entirely cured of her neurosis before it ended. This was also the opinion of the physicians who considered her case and, indeed, proved to be true.

At this point the case appeared, at first, to be satisfactorily ended, but I am sure that the questions which bothered us at the time have already arisen in your minds: Was not the cure effected by psychotherapy rather than by the correction of the anemia? Was not the statement, "All your symptoms are due to a trifling anemia and can be eliminated by four weeks of dieting" in itself sufficient mental stimulus to relieve her neurosis? Might not a pilgrimage to Lourdes have been as efficacious as the administration of liver and iron? Obviously we could not then answer these questions. In other words, the fact that the patient was symptomatically relieved by a régime which also improved the blood-picture did not fully confirm the hypothesis that the primary etiologic factor of her nervous disturbance was the anemia.

The subsequent history of the case, however, is exceedingly interesting and significant. During the cruise the patient continued to improve, and for a month was entirely free of nervous symptoms and able to do whatever she wished without fatigue. Then, suddenly, about three months after treatment was begun, and when she considered herself definitely cured, all nervous difficulties returned. There had been no change in the pleasant daily routine of the yacht; she was in splendid physical condition, eating well, sleeping well, and no longer tiring easily, and yet she suddenly found that she could not sit in the cabin with her husband and two friends without the old feeling of oppression, of crowding and dizziness, and weakness amounting almost to panic. She tried to convince herself that this was merely a transitory phase and to "stick it out," but at the end of a fortnight was forced to give up, and returned to seek medical advice in a much worse nervous state than at the time of her first visit.

Another blood examination was made, and it was found the hemoglobin had fallen to 60 per cent., the red blood-cell count had dropped nearly a million per cubic millimeter, and the red blood-cells again showed distinct features characteristic of so-called secondary anemia. Thus, again, there was a physical cause for the production of her neurotic symptoms, and this time we were even more certain that there was no psychologic etiology—all of which seemed to confirm the original hypothesis as to the origin of her first symptoms. From the purely organic point of view, however, no reason was found at first for the sudden recurrence of the anemia. There had been no abnormal blood loss, and she had continued to eat a very normal diet, with plenty of meat, fruit, and green vegetables, although she had, at our suggestion, stopped taking liver and had omitted the iron and cod-liver oil.

The problem, however, was soon solved, for she missed a menstrual period, and a few weeks later a definite diagnosis of a two months' pregnant uterus was made by the obstetrician. It is important to note here that the possibility of her being pregnant did not even occur to the patient until some time after the recurrence of her symptoms. By the time that the diagnosis of pregnancy was established, both the anemia and the neurotic symptomatology

had progressed to rather an alarming extent, and so after due consideration and the proper consultations—it was deemed advisable to terminate the pregnancy. As soon as this had been accomplished, she began to improve both functionally and organically. The progress was, naturally, less rapid than before, but was altogether satisfactory. Three months after her operation—her blood being entirely normal—she went to New Haven on a crowded special train, sat with 80,000 people at the Harvard-Yale football game, got caught in the crowd leaving the Bowl, and came back to Boston the same night without having experienced the slightest feeling of oppression or even subsequent fatigue. It is now three months since there have been any symptoms, the blood remains normal, and the patient has been leading a thoroughly normal and active life and is "perfectly relaxed for the first time in three years."

There is one minor point in the interpretation of the facts of this case which, for the sake of simplicity, I have left to the end. Preceding both the original neurosis and its recurrence there was an anemia during pregnancy. A discussion of the mechanism of this type of anemia is not a propos here. One cannot say whether the anemia or the mere debilities of pregnancy caused the neurosis. Both interpretations are tenable, but, for the purposes of this discussion, the question is unimportant, since, from either point of view, the nervous upset is to be considered the result of a physical factor.

Summary.—These 2 cases are presented to emphasize the importance of physical abnormalities, often of themselves of minor organic significance, yet of primary etiologic significance in the development of psychoneuroses. In Case I the fear of the pain of renal colic, the dread of instrumentation, and the anxiety over the possibility of operation produced a profound neurosis. In Case II a comparatively mild anemia related to a former pregnancy appears to have lowered the nervous resistance to such a level that a neurosis was established. This persisted until the blood returned to normal, and reappeared again when anemia developed accompanying another pregnancy. In neither case was there evidence that any other factors played a noteworthy rôle in the production of symptoms.

CLINIC OF DR. SOMA WEISS

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THE NATURE AND MANAGEMENT OF CEREBRAL HEMIPLEGIA IN PATIENTS WITH ARTERIAL HYPERTENSION

I DO not propose to present and discuss here[2] rare or obscure clinical manifestations, but rather to demonstrate certain frequently occurring clinical and morphologic pictures of cerebral complications in patients with arterial hypertension. If one considers that cerebral hemorrhage occurs more frequently and produces more severe damage to the central nervous system than the other neurologic conditions together, it becomes evident that the lack of proper familiarity of students and physicians with the nature and management of this condition is unjustified. The unfortunate results of the separation of clinical neurology from internal medicine manifest themselves more strikingly in this, than in other diseases.

PRESENTATION OF PATIENTS

The two patients before you were demonstrated two months ago. At that time, as you recall, both of them exhibited a number of identical symptoms and signs. Both patients were suffering for a number of years from abnormally high arterial blood-pressure, and both developed at about the same time a right-sided hemiplegia. The circulation was efficient, and the kidney function was normal in both patients. The sequence of events following the onset of the hemiplegia, and following the demonstration was quite different in the two patients. Patient I. G. recovered but partially, the improvement was slow, and at

[1] From the Fourth Medical Service.

[2] Medical Clinics of the Fourth Year Students of Harvard Medical School.

present, as a result of a second "shock," he is worse off than he was at the time when you saw him last.

Patient I. C., on the other hand, recovered within twenty-four hours after the onset of his hemiplegia completely, walked out of the hospital, attended his work, and developed a hemiplegia second time a few days ago. Following his second entry to the hospital the light hemiparesis cleared up again completely, and at present, as you see, he is mentally and physically fit.

We are dealing, then, with two patients who, as a result of hypertension, developed hemiplegia, one recovering promptly and completely, the other slowly and partially. *What is the explanation of this marked difference in the clinical progress of these two patients, and how shall we take care of them?*

Before answering this question let us, in recapitulation, briefly analyze the conditions of these two patients.

Patient 1.—I. G., a male storekeeper, fifty-three years of age, was admitted in a comatose condition to the Boston City Hospital on August 5, 1928.

The patient was found lying on the floor of his home in an unconscious state. On the following day, when he had partially regained consciousness, he informed us that about one hour before he was brought to the hospital he suddenly felt dizzy and weak, things began to turn around him, and he fell.

The patient had known for the last eight years that his blood-pressure was abnormally high. Occasionally he had pounding in the head, especially when emotionally upset. Of late he had worried a great deal because of financial difficulties, and when tired, experienced pressure sensations in his head. The past history as well as the social and marital history was unessential. Further inquiry brought to light the fact that the patient's father had died from a "stroke."

Physical examination on the day following his admission showed a semicomatose white man who appeared slightly younger than his stated age. The right pupil was larger than the left and both pupils reacted to light. The smaller branches of the arteries of the eye-grounds were tortuous and perhaps thinner and fewer in number than those of normal individuals. At the crossing of the arteries and veins the latter were found to be niched. The right side of the face was smooth, and an attempt to talk caused the mouth to be pulled toward the left. The neck was short. The thorax had a tendency to barrel shape, and moved but slightly with respiration. The left border of the heart in the fifth costal interspace was 12.5 cm. from the midline. The second aortic sound was ringing in character. The rhythm of the heart was regular, and the rate was 82 in one minute. The brachial, radial, and temporal arteries were palpable and slightly tortuous; they were thick rather than

hard. The right arm and leg were weak. The deep reflexes were increased over the right side. The abdominal reflexes on the right were absent. On the right side the Babinski reflex was present. The rest of the findings were unessential.

The systolic blood-pressure at time of admission was 250 mm. of Hg, the diastolic 150 mm. of Hg. During his one month's stay in the hospital the systolic blood-pressure fluctuated between 250 and 190 mm. of Hg, the diastolic between 160 and 90 mm. of Hg. The capillary blood-pressure as determined with a modified Recklinghausen capsule was 13 mm. of Hg (the average normal value is 8 mm. of Hg). The venous blood-pressure measured by the Moritz and Tabora method was 8 cm. of water (the average normal value is 5 cm. of water). The cardiac output was 6.3 liters of blood in one minute (average of three determinations. The average normal finding is 7.01 liters in one minute.) The stroke volume output of the heart was 74 c.c. (the average normal stroke volume is 78 cm.). The blood volume was 4.61 (the average normal blood volume is 5.81). The arm to face circulation time was twenty-five seconds as measured by the histamin method (the average normal value is twenty-three seconds). The respiratory minute volume was 7.81 (the average normal value is 6.1). The vital capacity 3200 c.c. or 1900 cm. per square meter of body surface (the average normal vital capacity is 4500 c.c. or 2500 c.c. per square meter of body surface). The respiratory quotient during the stage of fasting was 0.72. The oxygen consumption was 306 c.c. of oxygen per minute, or 85.2 calories per hour. The basal metabolism was +35 per cent. above the average normal value. The body temperature fluctuated between 97° and 98° F., the pulse varied between 75 and 100, and the respirations between 24 and 28 per minute. The hemoglobin content of the blood was 120 (Sahli). The white count was 14,800 per cubic millimeter of blood, and later 11,800 per cubic millimeter. The non-protein nitrogen was 35 mg. per 100 c.c. of blood. The Kahn test of the blood was negative. Repeated examination of the urine revealed a specific gravity of 1.011 to 1.012, a trace of albumin on three occasions after the hemorrhage. The urine specimens obtained after five days and later following the hemorrhage were free of albumin.

During his month's stay in the hospital he improved but slightly, the right-sided hemiparesis persisting and the muscle tone of the paralyzed side gradually increasing. There was evidence of mental deterioration.

Three weeks after the patient's departure from the hospital he was brought back with a history of again having dropped suddenly to the floor. The physical examination at the time revealed a more complete hemiplegia of the right side of the body. The patient showed no tendency to improvement during the past four weeks, and was distinctly losing ground. The pulse and respirations tended to rise and during the last two days the body temperature reached 100° F. At present he is suffering from hiccough which so far we have been unable to control. The rest of the clinical findings, at the present admission, were identical with those obtained during his first stay in the hospital, with the exception that the tone of the muscles of the right arm and leg is increased considerably and the patient tends to keep his right arm in an abnormally flexed state, with his leg in an extended position.

Patient 2.—A short résumé of the clinical condition of this patient is as follows: I. C., a sixty-two-year-old green-house worker, was admitted to the Boston City Hospital on September 15, 1928 in a semicomatose condition, talking rather incoherently. According to his foreman's statement the patient suddenly collapsed while working at his bench and lost consciousness. Following his stay in the hospital for a few hours the patient was able to give a clear and concise story. Four years prior to his present entry, while working, he suddenly became unconscious. The only premonition of this episode was a sensation of sudden "indigestion," dizziness, and thickness of speech for a few minutes previous to the collapse. At that time when he arrived at the admitting ward, he gradually regained consciousness but was unable to speak, and the right side of the body felt "dead" and paralyzed. Within twenty-four hours following his admission he felt well and was told by the physician that everything except his high blood-pressure was normal. After discharge from the hospital he returned to work, and save for occasional severe headaches, nosebleeds, dizziness, and "hearing the heart beats," he felt well. Six months ago he suffered from a similar attack, of shorter duration, however, than that described above. This attack, too, was preceded by vertigo and feeling of faintness. After rest he promptly recovered.

The other events in his past, social, and family history have no bearing on his present condition.

When examined shortly after arrival in the ward, it was observed that the arteries and veins of both eye-grounds were tortuous with occasional interruption of the veins at the crossing with the arteries. The arteries of the eye-ground had a greater opacity than in normal individuals. There was a slight weakness of the right side of the face. The speech was thick and blurred. The neck was rather short. He was barrel-chested with slight thoracic excursion and low position of the diaphragm, which moved but slightly with respiration. The cardiac apex impulse was barely perceptible in the sixth interspace, where the left border was 13.5 cm. from the midline. The heart sounds were slightly distant with the exception of the second aortic sound, which was conspicuously accentuated. The brachial, radial, and temporal arteries were tortuous and thickened. The radial pulses were of small excursion. The systolic arterial blood-pressure was 210 mm. Hg, the diastolic 110 mm. Hg.

There was a marked area of ecchymosis over the surgical neck of the left humerus, and the movements of the left shoulder-joint were limited.

The muscular power was weaker over the right side of the body, where the deep reflexes were increased. A fatigable ankle-clonus and Babinski were elicited over the right foot. The rest of the physical signs were of no significance.

During his two weeks' stay in the hospital the systolic blood-pressure fluctuated between 180 and 210 mm. Hg, the diastolic blood-pressure between 90 and 110 mm. Hg. The pulse varied from 80 to 95, and the respirations between 23 and 28 in one minute. There were 4,700,000 red blood-cells in a cubic millimeter of blood, and the hemoglobin content was 85 per cent. The platelets and the shape of the red cells were normal. The white blood-cell count was 17,200 in 1 cu. mm. of blood on the day of admission. Of these

white blood cells, 77 per cent. were polymorphonuclears, 16 per cent. lymphocytes, 6 per cent. large monocytes, and 1 per cent. basophilic cells. The white blood-cell content of the blood was 12,600, 10,000, and 11,000 at two-day intervals respectively. The non-protein-nitrogen content of the blood was 36 mg. per 100 cm. The Kahn test of the blood was negative. The urine showed a fluctuation in the specific gravity from 1.015 to 1.030. Abnormal constituents were not detected. The phenolphthalein output in two hours was 35 per cent. of the amount injected.

The day following his admission to the hospital the weakness disappeared completely and the patient mentally became normal also. He stayed in the hospital for two weeks.

Four weeks following discharge (four days ago) he developed a spell of unconsciousness similar to that just described. Within a few hours after his re-entry to the hospital his condition cleared up completely once more, and now, as you see, except for his chronic cardiovascular ailment, he is normal.

Comments.—1. Among the *symptoms* exhibited by the two patients prior to the occurrence of the cerebral complications there are a few which, though not specific to *arterial hypertension,* nevertheless make us suspect and exclude the presence of this disease if they occur in or after middle age. Frequent and rather severe headaches associated with sensation of fulness, and pulsation in the head, worse during emotional upset and fatigue; short dizzy spells; blurring of vision; noises in the head synchronous with the heart beats; are frequent complaints of patients with arterial hypertension. A recent analysis of 412 ambulatory patients of the Out-patient Department of this hospital, who suffered from abnormally high blood-pressures, revealed that there are no symptoms specific for, or even strongly suggestive of, arterial hypertension. The following are the most frequent symptoms occurring alone or in combination with others: pains and aches (44.6 per cent. of the cases); dizziness (39.3 per cent.); headaches (34.2 per cent.); dyspnea (34.2 per cent.); nocturia (25.5 per cent.); palpitation (16.1 per cent.); weakness (13.3 per cent.); tinnitus (11.6 per cent.); epistaxis (5.3 per cent.). Only 12.1 per cent. of the cases were entirely symptomless. It is evident, of course, that there is a greater number of patients who, merely because they are symptomless, do not seek the aid of the physician, and therefore do not fall within this group.

The combination of symptoms of patients with arterial hypertension is similar to those of psychoneurotic individuals.

Whether or not psychoneurosis is really an important causative factor in arterial hypertension cannot be stated with any justification from the above data alone. Similarly, one cannot state whether some of the symptoms occurring in patients with hypertension are the result of hypertension, or whether they are the manifestation of an underlying constitutional personality. One would suspect that "pulsating, splitting headaches," associated with pressure sensation in the head and ringing in the ears, worse during mental or physical exertion, are among the symptoms most suggestive of arterial hypertension.

2. Some of the *physical signs* exhibited by these two patients have direct hearing on *arterial hypertension*. The changes in the vessels of the eye-grounds, the short neck, the tendency to barrel-shaped chest with rather limited respiratory movement and the low level of the diaphragm, the accentuated ringing second aortic sounds, the small but forceful radial pulse, the palpable larger arteries are frequently associated with hypertension. The combined occurrence of these signs enables one, with a little clinical experience, to diagnose the disease with a fair degree of certainty.

3. Among the *laboratory observations* bearing on *arterial hypertension*, it is of significance that the cardiac output per minute, the mean velocity of the circulation, as well as the arm to face velocity of the blood, were not above the normal values. On the contrary, the results of these measurements were slightly lower than those obtained in normal individuals. Similar findings were obtained on 18 additional cases of arterial hypertension in a study in progress by Dr. Lawrence B. Ellis and me. These findings, together with the presence of normal or slightly elevated capillary and venous pressure, indicate that the heart works against a considerably increased resistance in arterial hypertension. The resistance is probably between the larger arteries and capillaries. With Dr. Lawrence Ellis we have obtained experimental evidence which indicates that the arterioles, on which histamin exerts a specific action, are in a functional spasm in arterial hypertension. It is very suggestive that anatomic changes in the arterioles, in addition to the functional

spasm, may be present in a number of cases. *According to this conception the increased blood-pressure is a functional compensation of the heart to maintain a normal capillary circulation in the presence of the spasms of the arterioles.*

The basal metabolism in patient I. G. was +35 per cent. It is recognized that one group of hypertensive patients have high oxygen consumption. These patients often give clinical evidence of an overactive sympathetic nervous system.

4. *Symptoms Referable to Cerebral Hemiplegia.*—It is not a coincidence that these patients with *arterial hypertension* felt suddenly dizzy, nauseated and weak just before collapsing as a result of the "*cerebral complication.*" While damage in the brain, as a result of rupture of a large artery, may develop so suddenly and extensively that it precipitates collapse without warning (foudroyant apoplexy), this manifestation is a rather rare one. More often, coincident with or shortly preceding the onset of vascular change *prodromal symptoms* may be present, as in Patient I. C., or, in addition, a sensation of "rush of blood into the head," of "seeing black" or paresthesias. Such symptoms may precede the collapse and coma by a few minutes or several hours. More significant than these *symptoms* are those which occur *earlier* and which, if the patient is intelligent and reliable, can be elicited quite frequently in the history. For days or weeks before the onset of the cerebral accident the patient may complain of severe, lasting, and more frequent headaches than usually. He becomes very irritable, or hilarious, a condition which can seldom be explained by the family or friends. Sleeplessness is often present. The patient may often notice that he is "tense." Because the importance of recognition of the significance of these complaints, I wish to cite, as an example, the description of the symptoms of a missionary whom I have seen recently, a year after he developed a hemiplegia in India. "I have known for years that my blood-pressure was high. A month or two previous to the occurrence of the shock I had worked unusually hard. In addition to this, I worried more than usual because of certain principles adopted by the leaders of the mission. I was tired. I was tense. Upon the least provocation I

became irritated at my closest friends. When I quieted down I felt humiliated and surprised at myself. The week before the shock occurred I told my friends that I must take a vacation or I should 'break.'"

I am quoting this statement because it is certain that physical and emotional overexertion hastens and precipitates cerebral accidents in a considerable number of instances. In recognizing this important principle, possibilities are given us to apply the most significant therapeutic measures to patients with hypertension. Preventive measures, such as physical and mental rest, may help temporarily or permanently to prevent the occurrence of cerebral accidents, I shall return to this later in discussing the management of cerebral accidents.

5. The *neurologic signs* exhibited by these patients are the most frequently observed manifestations of *cerebral hemiplegias* associated with hypertension. It is out of place here to go in detail into the interesting and difficult field of finer localization of cerebral hemorrhages of patients with arterial hypertension. A few facts, to be mentioned here, nevertheless, will aid to solve the diagnostic problem of a large number of patients. To learn of cases where reservation, caution, and refined skill in diagnosis is necessary, requires long experience and careful checking of one's mistakes by the autopsy table.

In the very severe and massive hemorrhages the patient is in deep coma, the face is flushed, the respiration is labored with a quite characteristic puffing of the mouth. There is complete motor and sensory paralysis and the reflexes are abolished. The temperature may be subnormal or highly elevated. In this stage exact localization may be impossible.

If the face is smooth and the patient puffs more on the affected side; if the abdominal reflexes are absent and the Babinski or other equivalent reflexes are present on the same side; and if the elevated leg with a low muscular tone drops down in a "dead way" without subsequent movement; if, in addition, the head and eyes turn to the opposite side (conjugate deviation) to the one with neurologic signs; the bleeding is present in the hemisphere corresponding to the side toward

which the head and eyes are turning. A combination of a few of these signs should often suffice to diagnose and localize the seat of the "cerebral accident." In addition to the favorite location of cerebral hemorrhage in the internal capsule and in the basal ganglia, hemorrhages may occur less frequently in the pons, cortex, cerebellum, and medulla.

The most affected movements in patients with hemiplegia are those which are naturally unilateral. The highly specialized movements which are of late development, are more affected than the more primitive ones. Movements of the muscles of the neck and trunk, concerned in the automatic maintenance of the erect position, are often little affected as compared with those of the limbs. The automatic respiratory movements on the affected side may be greater, but when forced respiration is made the asymmetry is reversed. As a rule the function of the arm is more involved than that of the leg, and that of the fingers more than of the shoulder and elbow. In the latter course of the disease involuntary adduction and internal rotation of the shoulder, flexion and pronation of the elbow; and flexion of wrist and fingers are the often assumed characteristic positions. The lower extremity of the affected side becomes extended with the foot acquiring an equinovarus position. Walking is made difficult by the tendency of the toes to catch the ground. The patient learns to overcome this obstacle by circumducting the leg at the hip when he advances.

The further manifestations of cerebral hemiplegia vary considerably. Rise in temperature, as observed in patient I. C., is usually an evidence of serious complication during a cerebral hemorrhage. The cause of death in the majority of patients with cerebral hemorrhage is bronchopneumonia. The exact mechanism of this bronchopneumonia is not clear at present. It is very suggestive that, with the cerebral hemorrhage, *marked vasomotor disturbances* are present. The deeply *engorged lungs if associated with cerebral hemorrhage*, in instances when the patient dies before there is an opportunity for development of a bronchopneumonia, is often so characteristic at postmortem exam-

ination that one may foretell from the appearance of the lungs the presence of severe trauma to the brain.

6. Among the *laboratory findings, bearing on the cerebral complication* of the two patients with arterial hypertension, the *leukocytosis* and the temporary appearance of glucose in the urine are of interest. Leukocytosis often is present following cerebral hemorrhage. The leukocytosis is apt to be specially marked in subarachnoid and intraventricular hemorrhage.

Different types of sudden traumatic injuries to the brain may result in the appearance of varying amounts of *glucose* in the urine. Occasionally the glycosuria may be associated with temporary marked hyperglycemia. I observed patients in whom even acetone and diacetic acid appeared in considerable amounts in the urine following a subarachnoid hemorrhage. These facts would indicate that in intracerebral, as well as in subarachnoid hemorrhage, the carbohydrate metabolism may be considerably disturbed temporarily.

THE CORRELATION OF CLINICAL MANIFESTATIONS AND THE MORPHOLOGIC AND FUNCTIONAL CHANGES IN THE BRAIN OF PATIENTS WITH CEREBRAL HEMIPLEGIA

The various types of hemiplegias from the point of view of prognosis may be grouped in the following arbitrary way. (A) Hemiplegias with sudden onset and permanent damage. (B) Hemiplegias with sudden onset and subsequent slight improvement only. (C) Hemiplegias with sudden onset and subsequent slight permanent damage. (D) Hemiplegias with sudden onset and complete recovery, within a few days or hours. (E) Hemiplegias with slow onset and permanent damage.

To foretell at the time of onset of the hemiplegia with which of the above possibilities we are dealing is impossible.

If one attempts to correlate the clinical manifestations and progress of the patients, with the extent of demonstrable morphologic damage in the brain, one is impressed by the frequent lack of such correlation. In the type of hemiplegias falling into *Groups A*, *B*, and *C* it is almost certain that, aside from the evidence of permanent damage as the result of a hemorrhage or is-

chemia due to occlusion of a large vessel, temporary morphologic and perhaps functional disturbance of the brain tissue may play an important rôle. Temporary edema, compression, vascular spasm involving brain areas of varying size developing in connection with the permanent and demonstrable damage, are factors which are responsible for the lack of obvious correlation between morphologic pathology and clinical manifestation in cases of hemiplegia.

The functional and morphologic correlation of patients with complete recovery (*Group D*) is obviously even more difficult, for opportunity of observing the brain during the hemiplegia is but slight. The evidence available today suggests that small hemorrhages, perhaps thrombosis of small vessels, and temporary spasm of the cerebral vessels may be causative agents in these cases. I am of the opinion that both small hemorrhages due to rupture or thrombosis of minute vessels and spasm of the cerebral vessels are probably responsible for a number of such hemiplegias, as is also, for example, the one demonstrated on patient I. J. Minute single or multiple cerebral hemorrhages in patients with arterial hypertension are not rare occurrences. I shall demonstrate later a specimen of brain with such minute hemorrhages. Often where an extensive single hemorrhage is diagnosed multiple, hemorrhages are found. Why such hemorrhages should be multiple and occur simultaneously is difficult to understand. One of the explanations is that the arterioles of a larger arterial branch develop a spasm, and because the presence of degenerative processes in these arterioles (arteriolosclerosis) they are unable to withstand the abnormally high pressure. In addition to the multiple punctate hemorrhages resulting from the rupture of minute blood-vessels, multiple hemorrhages as a result of thrombosis of the arterioles and secondary extravasation of the blood are observed in patients with hypertension. These thromboses are apt to occur during a period when the unusually high blood-pressure which is necessary to maintain a normal capillary flow falls rather abruptly, *without a corresponding relaxation of the arterioles*. We have demonstrated that the high blood-pressure in patients is best suited to maintain

a normal capillary flow. If this optimal blood-pressure falls with persistent arteriolar spasm, circulatory stasis may develop. Circulatory stasis in a vascular area with diseased intima of the vessels is one of the conditions most favorable to the formation of thrombosis. The fact that these transient hemiplegias are apt to occur at night when the blood-pressure falls, favors this conception.

It is then obvious that these small hemorrhages with the adjacent edema and pressure may completely paralyze a large brain area. The edema and the small hemorrhages are rapidly and completely absorbed later, and recovery occurs. The *healing capacity of the brain* from traumatic injury is probably not less than that of other tissues. One often has an opportunity to gather evidence supporting this, especially in medicolegal practise, by observing specimens of brain where there are repeated injuries (chronic alcoholism) with only slight scar tissue formation and with complete functional restoration.

The question as to whether the *cerebral vessels* may go into *spasm* is a long debated problem. The vasomotor reactions of vessels of the brain of animals were confirmed and denied repeatedly. The different results of the investigators depended probably on the experimental condition of animals. During the past decade, on the strength of observations on animals, the conception that the human brain vessels did not possess appreciable vasomotor play became prominent. During the past year with Dr. George P. Robb we obtained direct evidence that the minute vessels of the brain, especially the arterioles, possess a marked capacity for constriction and dilation. Observations with histamin indicate that *the arterioles of the human brain are sensitive to unusually small amounts of histamin*, and their sensitivity surpasses that of the arterioles of almost any organ, with the exception of the vessels of the face. These findings are substantiated by recent experiments on animals by Cobb, Forbes, and Wolff at the Harvard Medical School. The rôle of temporary cerebral spasm, "vascular crisis," is suggestively supported and defended also by histologic studies of Spielmeyer of Munich.

It is clinically recognized that patients with high arterial

blood-pressure are apt to show an unstable vasomotor system. From this and the foregoing discussion it is most logical to believe that *a disproportion between cerebral arteriolar spasm and systemic blood-pressure*, which favors the development of a *cerebral ischemia*, is responsible for these *transient hemiplegias*. It is, of course, obvious that in the production of this disproportion, fall in the systemic blood-pressure, increased localized spasm of the arterioles, or various combinations of these two factors may be responsible in different individuals. Transient thrombosis of the cerebral vessels is a more frequent complication in patients suffering from arterial hypertension and cerebral arteriosclerosis, than is recognized at present.

POSTMORTEM DEMONSTRATION OF BRAINS OF PATIENTS WITH HEMIPLEGIAS

The lesions in the brain in cerebral hemiplegias and their relation to the clinical manifestations are of such importance that it may be of interest to demonstrate here a few types of the cerebral lesions which occurred as a result of arterial hypertension and associated arteriosclerosis.

The *first specimen* (Figs. 10, 11) was obtained from patient T. M., aged forty-seven, who had been suffering from arterial hypertension for a number of years. On March 24, 1928 he suddenly collapsed while on a step ladder, and fell instantly into deep coma. He was brought to the hospital, and from the time of his admission until death, sixteen hours later, he failed to respond to any stimulation. The eyes and head were turned toward the left and all the clinical signs, described before, which are characteristic of a massive cerebral hemorrhage of the internal capsule of the left hemisphere, were present.

Let us see now the corresponding anatomic picture.

On removing the brain from the calvarium, the first striking feature is the complete flatness of the gyri and obliteration of sulci of the surface. In addition, there is definite bulging of the parietal aspect of the left hemisphere. On separating the two hemispheres longitudinally (Fig. 10) clotted blood appears from the lateral ventricles. A transverse section of the left hemisphere indicates

that a surprisingly large portion of brain matter (Fig. 11), including the internal capsule and the basal ganglia, is completely destroyed. On carefully washing away the blood and the débris of brain tissue we observe that the arteria fossæ sylvii, or rather one of its small branches, is ruptured. From this finding one clearly understands the clinical behavior of this patient.

It is surprising what a degree of destruction may result from the rupture of such a small artery. The lenticulostriate and

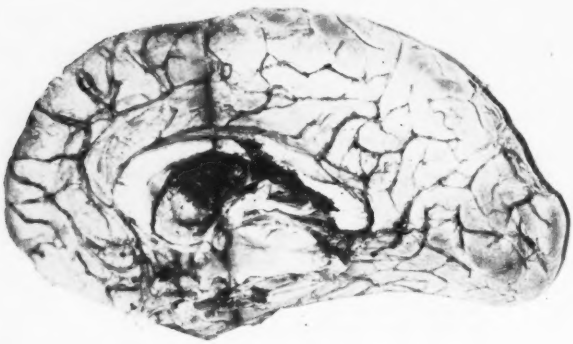

Fig. 10.—Patient T. M. Inner surface of the left hemisphere with hemorrhage into the lateral ventricle resulting from a massive hemorrhage into the left internal capsule.

lenticulo-optical branches of the arteria fossæ sylvii are favored sources for cerebral hemorrhages. They rupture in about two-thirds of the total cases of spontaneous intracranial hemorrhage. One reason for this may be that these arteries branch in an angle of 90 degrees from the main vessel, and if, in addition to the hypertension degenerative processes develop, they are apt to form miliary aneurysms.

The *second specimen* is the brain of C. K., aged fifty-three, who died as a result of lobar pneumonia. In this patient we have an opportunity to observe the clinical and morphologic end-result of a hemiplegia from which the patient recovered to a large extent. The cerebral accident resulting in a right hemi-

paresis and sensory and motor aphasia occurred *seven months before his death.* Within one month the patient recovered almost completely, with the exception of his speech. A partial motor aphasia persisted until death.

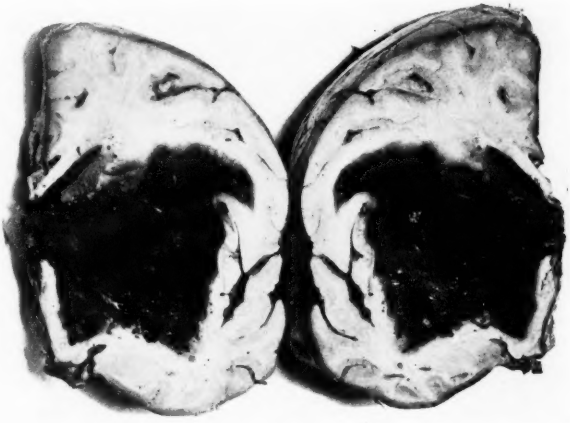

Fig. 11.—Patient T. M. Midtransverse section of the left hemisphere showing the destructive effect of a massive fresh hemorrhage into the internal capsule.

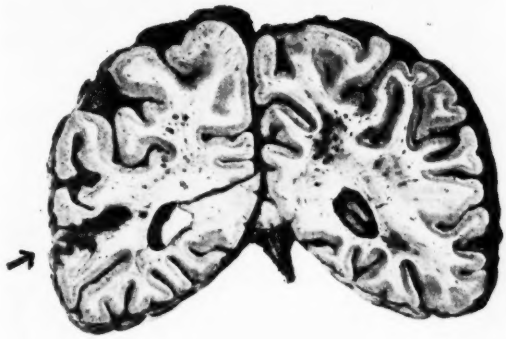

Fig. 12.—Patient C. K. The small cyst ("plaque jaune") behind the lower portion of the central gyrus is the residuum of a small hemorrhage which occurred seven months previously.

In sectioning the brain, as you see, the only abnormal finding in addition to the marked arteriosclerosis is a *yellow cyst*, starting at about 1 cm. below the surface of the lower portion of the anterior central gyrus. The cyst is about 2 x 1 cm. (Fig. 12). The clinical and anatomic correlation in this patient indicates that only the structures of the speech center were permanently damaged in this instance, and the reason that the patient recovered so completely from the rest of the hemiplegia lies in the fact that the other nerve structures were only temporarily paralyzed, probably as a result of pressure and edema.

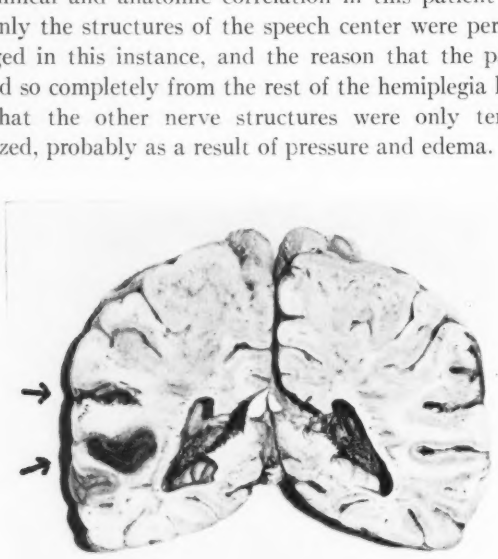

Fig. 13.—Patient S. Mc. Two small hemorrhages in the left hemisphere. The upper and smaller lesion is the remains of a hemorrhage one and a half years ago. The lower hemorrhage occurred two weeks before death.

The yellow cyst ("*plaque jaune*") is a characteristic residuum of an old hemorrhage. At the site of hemorrhage hemoglobin gradually changes to other pigments, with organization and liquefaction of the destroyed area.

The *third specimen* to be demonstrated is the brain of patient S. Mc., aged forty-three, who was treated in the Out-patient Department for high blood-pressure. He had suffered from a "shock" one year ago, with the result of a right hemiparesis. From this he recovered gradually and completely, and two weeks

ago, while under treatment for severe nephritis, a second "shock" developed. The patient died with the symptoms of uremia.

On sectioning the brain, below the middle portion of the posterior central gyrus, a small yellow plaque as residuum of the old hemorrhage is present. Below this there is a small circumscribed fresh hemorrhage (Fig. 13). This specimen illustrates one hemorrhage from which gradual and complete recovery occurred. The second and recent hemorrhage gave no evidence for definite localization. Often one observes *repeated cerebral* hemorrhages in the same person with marked recovery from each attack.

The *fourth specimen* of brain is that of A. M., aged fifty, who, as a result of arterial hypertension, developed a circulatory fail-

Fig. 14.—Patient A. M. Multiple punctate hemorrhages in the left cerebellar lobe.

ure. He had suffered from left hemiparesis four weeks before his death from which he recovered promptly within a few hours. He died as a result of bronchopneumonia. At autopsy the cerebrum was essentially normal, except for arteriosclerosis of the large vessel, and the left hemisphere of the cerebellum showed numerous scattered punctate hemorrhages (Fig. 14). Apparently no symptoms or signs were observed as a result of these multiple hemorrhages. We are unable to state whether the transient hemiplegia was due to similar punctate hemorrhages observed in the cerebellum, or to spasm. At the time of death

the right cerebral hemisphere was grossly normal. I am demonstrating this specimen because such multiple punctate hemorrhages are one of the types of cerebral damage occurring in patients with arterial hypertension.

The *fifth specimen* of brain was obtained from M. L., aged sixty-four. The clinical course of this patient, as well as the nature of lesions in the brain, is more unusual, and therefore I shall give the clinical picture in greater detail.

The patient was admitted to the hospital on November 29, 1928, *complaining* of severe pain in the occipital region. The onset of this pain was sudden, three days previously, while the patient was lifting two medium sized pails of coal. The sharp pain radiated from the occipital region to the neck. The pain was constant since onset and became accentuated on motion of the head in any direction. She also suffered from severe generalized headaches. She had suffered from a left hemiplegia with a sudden onset one and a half years before, from which she cleared up completely. The rest of the history bore no relation to the present illness.

At the time of admission she was but slightly drowsy and answered questions intelligently but perhaps rather slowly. There was a slight left facial weakness. The left pupil was slightly larger than the right. The arteries and veins of the fundi were tortuous. The heart was enlarged. There was no paresis, but on the left side the Babinski and Oppenheim reflex was positive.

Three days later the general condition was unchanged, with the exception that the patient became slightly more drowsy.

Seven days after admission the left upper extremity became completely paralyzed. Definite evidence of early choking of the disks appeared. The Babinski reflex was now positive on both sides.

Nine days following admission the patient was in coma. The breathing had become stertorous, the head and eyes were pulled toward the left, and there was a flaccid left hemiplegia. She died December 9, 1928. Among the *laboratory tests* the significant findings were: The presence of 20,000 white blood-

cells per cubic millimeter of blood on admission, which rose to 36,000 before death; the differential white count was 80 per cent. polymorphonuclears, 12 per cent. lymphocytes, and 8 per cent. monocytes; the spinal fluid pressure three days after admission was 400 mm. of water, 460 mm. of water when exerting pressure on the right jugular vein, 470 mm. of water when exerting pressure on the left jugular vein, and 500 mm. of water when pressing on both. The fluid was cloudy and pink with 5600 red blood-cells and 100 white blood-cells per square millimeter. The

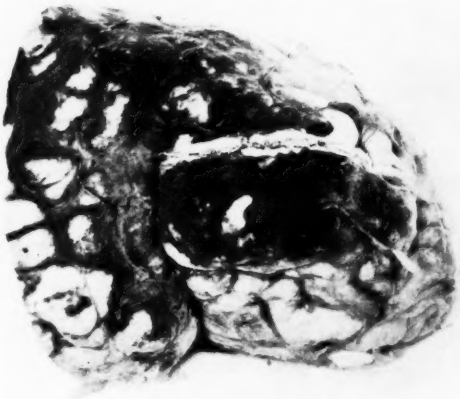

Fig. 15.—Patient M. L. Outer aspect of the anterior half of the left hemisphere with extensive subarachnoid hemorrhage.

pressure of the spinal fluid eight days later gradually subsided to 120 mm., following several punctures. The red cell count was 3200 per cubic millimeter of spinal fluid. The Wassermann of the spinal fluid was negative. The urine contained albumin and casts after onset, but these findings were later absent.

At postmortem examination of the body, on removing the brain from the calvarium, the vessels of the base showed marked arteriosclerosis with irregularly scattered calcific plaques. The surface of the brain over the left side, and partially over the right, was suffused with black color as a result of a *diffuse sub-*

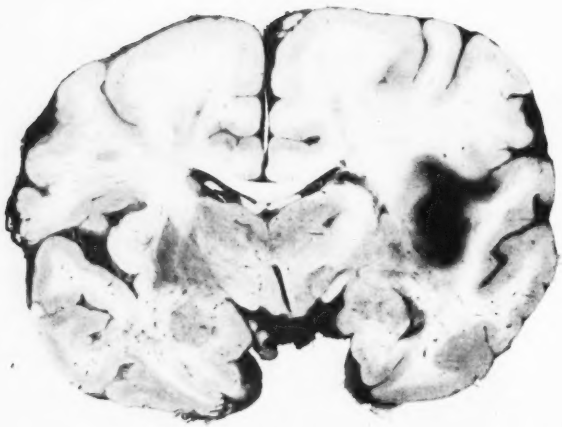

Fig. 16.—Patient M. L. Posterior view of a cross-section corresponding to the anterior portion of the island of Reil. The subarachnoid hemorrhage considerably separated the sylvian fissure on both sides and the structures around the island of Reil. There was no evidence of intracerebral hemorrhage.

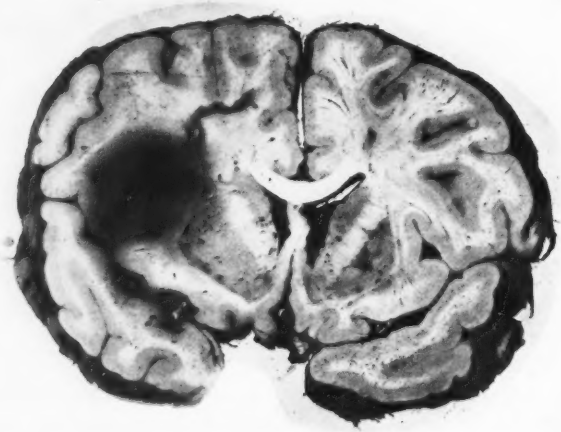

Fig. 17.—Patient M. L. Anterior aspect of a cross-section corresponding to the middle portion of island of Reil. The subarachnoid hemorrhage exerts considerable pressure of the structures around the island of Reil with transudation of blood into the brain tissue close to the surface.

arachnoid hemorrhage (Fig. 15). The serial cross-section of the brain showed the subarachnoid hemorrhage extending to both sides, and was especially thick, producing considerable compression and transudation of blood-pigment into the brain tissue around the island of Reil (Figs. 16, 17). No evidence of intracerebral hemorrhage was found.

The unusual feature of this case is that at onset the patient's prognosis was not considered serious, and it was obvious that we were dealing with a spontaneous meningeal hemorrhage. The patient then gradually developed signs of complete hemiplegia and died. The postmortem findings did not reveal a second lesion in the internal capsule, which was free from hemorrhage. The pressure due to the extensive subarachnoid hemorrhage around the right sylvian fissure and island of Reil (Figs. 16, 17) exerted sufficient pressure and edema in the right internal capsule to cause a left hemiplegia, coma, and respiratory paralysis.

THE PROGNOSIS IN CEREBRAL HEMIPLEGIA

The prognosis in the early stage of hemiplegia is difficult and often it is not more than mere guess work. To foretell whether the loss of function is due to destruction of brain tissue, pressure, edema, vascular spasm, arteriolar thrombosis, or to a certain combination of these factors is impossible at the onset. Our attitude should be, therefore, a hopeful one.

There are a few general helpful leads. The deeper and longer the duration of the coma, the more hopeless is the prognosis. A coma lasting over twenty-four hours is of grave significance. Marked drop or elevation in the temperature soon after onset is of bad prognostic significance. If evidence is established that the hemorrhage broke into the ventricle, the chances for recovery are slight. Progress during the first week will also aid us in foretelling the fate of the patient. The more progress is made during the first few days, the more probable it is that the hemiplegia is due to indirect changes.

THE MANAGEMENT OF PATIENTS WITH HEMIPLEGIA

Preventive Measures.—The general care and treatment of patients with arterial hypertension bear directly on the prevention of cerebral accidents. The treatment of the high blood-pressure is not important only because it may lead to cerebral hemorrhage per se, but because it predisposes to hemiplegia by causing diffuse vascular degeneration. In addition to specific treatments which are advocated at present—such as nitrites, sulfocyanate, low protein and salt-free diet—the general care of the patient will be beneficial. If the patient is overweight his caloric and water intake should be reduced. It is of the utmost importance to establish physical and mental rest. The condition and social status of the individual will determine how this rest will be inaugurated. It should be emphasized here once more that no strenuous effort should be made to promptly reduce the blood-pressure. It was shown that the reduction of blood-pressure was beneficial only if it were the result of *arteriolar relaxation.* A therapeutic measure which reduces the blood-pressure without decreasing the peripheral resistance is apt to be harmful and will predispose to cerebral ischemia, edema, and thrombosis.

A considerable number of patients suffering from hemiplegia shows evidence of a rather unstable psychic make-up with mental tenseness. The value of *rest-cures* in arterial hypertension is but little appreciated at present. Two to four weeks of absolute physical and mental relaxation two or three times a year is very beneficial in these patients. In order to prevent abnormal emotional fluctuations, sodium bromid, gr. x (0.6 gm.) three times daily, or luminal, gr. $\frac{1}{2}$ to gr. 1 (0.03 to 0.06 gm.) in the morning and evening, taken for four weeks and then abandoned for an equal length of time, may be advisable. Potassium iodid, administered perhaps during the period when the sedatives are not taken, may serve as a preventive agent. Gradually increasing doses up to 5 grains (0.3 gm.) three times a day may be administered. It should be remembered, however, that the rational use of iodids in arteriosclerosis is not proved at present. The consumption of alcohol, nicotin, and caffein should be restricted

as indicated. As a considerable number of patients with arterial hypertension suffer from constipation this condition should be relieved; aloe, strychnin, and phenolphthalein mixtures taken regular are often useful.

These principles of preventive treatment should be applied also in patients recovering from cerebral hemorrhage, for it is recognized that there is a tendency for recurrence of such attacks.

Management of the Patient with Hemiplegia.—Immediately after onset of the "shock" the proper management of the patient is of great consequence. The intracranial changes during the first few hours following onset will determine the extent of the permanent damage to the patient. Rash measures may cause considerable damage.

When the patient is seen immediately following the onset of the hemiplegia, the clothing should be loosened, particularly around the neck. The head should be slightly elevated, and it may be advisable to turn it toward one side in order to prevent the tongue from slipping backward. In the event that *convulsions* are present, these should be stopped as promptly as possible. During the convulsive seizure the intravascular and intracranial pressure is considerably elevated, and therefore it may increase the cerebral damage, and it may also hasten respiratory paralysis. In my experience morphin and large doses of bromids have been ineffective in stopping such convulsions. The intelligent intravenous application of sodium luminal has proved of great service in our experience. Sterile ampules containing 2 grains of the medication (prepared by the Winthrop Chemical Company of New York City) are dissolved in water containing 1 per cent. of the drug. Of this, 5 grains are injected, and the effect observed for fifteen minutes. If, after the elapse of this period, the convulsions still persist, further dosage of 2 grains at ten-minute intervals may be injected up to 12 grains. I have experimentally observed that similarly to the behavior of morphin, *in irritative states of the central nervous system, larger amounts of luminal are required to induce sleep. On the other hand, depression of the centers acts synergistically with the sedative action*

of the luminal, and other barbituric acid derivatives. For this reason, in cerebral hemorrhage caution is advisable in the application of luminal; for at the onset one does not know the degree of depression which may follow. The advantage of the intravenous application of sodium luminal is that its effect is instantaneous; that the sleep induced is not deep, as the patient maintains the reaction to painful stimuli; it lasts four to twelve hours; and the heart and blood-pressure are not influenced appreciably. I have administered in epilepsy major, tetanus, delirium tremens, and severe procain poisoning with repeated convulsions, a solution of sodium luminal by vein slowly and continuously ($\frac{1}{2}$ grain per minute), until the patient relaxed and fell asleep. This occurred after the administration of between 7 and 14 grains.

The transfer of the patient to bed should be performed with the greatest care. In bed, the head, neck and chest should be slightly elevated, strong lights and noise should be excluded from the room, and in the event that the patient awakens, voluntary movements should be discouraged. Application of an ice-cap over the affected hemisphere is a harmless procedure with possible beneficial effect. If the blood-pressure is very high, *venesection* should be considered, and 500 to 700 c.c. of blood removed. Administration of calories during the first twenty-four hours is not important, but the normal *fluid intake* should be maintained by rectal or subcutaneous channels. This is especially important because at the onset of hemiplegia the pulmonary ventilation and with it the water evaporation are greatly increased. No attempts should be made to arouse the patient from his coma. After the elapse of the first day, if the patient's general condition has improved, feeding should begin, but special attention should be exerted that food particles should not enter the trachea. The *danger of bronchopneumonia*, which is the most frequent cause of death, is especially great during the first week. The mouth should be kept clean. The patient's position in bed with active support should be changed frequently. This change in position helps to prevent not only bronchopneumonia, but also *bed-sores*, which are one of the complications to be avoided. Careful nursing and hygiene of the

skin will be of additional help in preventing bed-sores. Retention of urine during the first one or two weeks requires the use of the catheter. Rigid asepsis here is self-evident. Disturbances in the gastro-intestinal function may manifest themselves in incontinence with diarrhea or constipation. Daily enemas are helpful.

There is a small group of patients, who with advancing age and marked arteriosclerosis, usually coincident with a fall of blood-pressure due, as discussed before, to myocardial fatigue, develop hemiplegia as a result of arterial or *multiple arteriolar thrombosis*. The diagnosis of these hemiplegias, at the onset, is very difficult and therefore rational treatment can be applied only if the rapid improvement of the hemiplegia, the negative findings of the spinal fluid, and often the history of similar attacks make the diagnosis plausible. In these patients elevation of the foot of the bed, in order to raise the cerebral venous, and thereby the cerebral arteriolar, pressure, is advisable. Digitalis in tincture or powder form should be administered. It is useful to administer the digitalis promptly, for if the blood-pressure and the efficiency of the cerebral circulation are re-established with expediency, a re-establishment of the blood flow may occur. Of the tincture of digitalis, a total dose of 2 minims (0.15 c.c.) for each pound (0.45 kg.) should be given, in four divided doses at six-hour intervals. Other cardiac stimulants may also be considered.

In all patients about two weeks following onset, if complications do not contraindicate it, gentle massage of five minutes' duration may be instituted. This massage should be lengthened and made stronger. Later the patient should be encouraged to massage the lame side himself.

As soon as the patient's general condition becomes satisfactory, certain motions return, and if he has a desire to leave the bed, he should be permitted to sit up. The presence of a physician when the first effort is made to use the paralyzed side is advisable. Active support and encouragement should aid the patient during these attempts, which should not last over a few minutes at the beginning, and should increase gradually.

In addition to the massage passive motion of the joints should be introduced.

As contractures are especially apt to involve the flexors of the forearm, fingers, and hand, the abductors and the inward rotator muscles of the upper arm, and the dorsal flexors of the feet, special attention should be paid that the arm and fingers should early be kept extended, the hand in supine position extended, the upper arm in abduction and extended rotation, the thigh abducted, the knee flexed, and the feet in dorsal flexion.

Any additional exercises will depend on the functional disturbances of the individual patient. Training in walking, in certain simple grasping movements, and in writing, are of useful importance. Application of an Esmarch bandage may aid in overcoming the disturbing spasm during exercise.

Electrotherapy has but doubtful value, and its moral effect is to discourage the patient to make efforts of his own will. Similarly, the application of various baths advocated have no proved beneficial effect. Cold and hot baths should be avoided in all circumstances.

Surgical decompression for relief of the intracranial pressure, as well as surgical attempts to remove the blood-clot, have been made in the past, without definitely proved usefulness. Special indications for such use, however, may develop.

The problem of application of spinal punctures as a diagnostic and therapeutic procedure is not settled. The frequently mentioned argument against the application of this procedure is that it may hasten the extension and possible rupture of the hemorrhage into the ventricle. It is questionable whether this argument is of practical validity. During a cough, defecation, and other muscular efforts a more marked fluctuation in the cerebral pressure develops than during a carefully and slowly conducted spinal puncture. Besides, there is a probability that the slow reduction of the spinal pressure is useful. In subarachnoid hemorrhage this is quite definite. If one considers, furthermore, that the diagnosis is often not clear in these patients, one is apt to think that we are much too conservative in

the application of spinal punctures. Future clinical studies on this problem will serve a useful purpose.

SUMMARY

The most frequent clinical manifestations of cerebral hemiplegia in patients with arterial hypertension, with or without associated arteriosclerosis, have been demonstrated. The significance and interpretation of symptoms and signs of patients, as well as the laboratory findings in this condition, have been discussed. The correlation between the functional and morphologic changes in the brain and the clinical picture of hemiplegia have been analyzed. The morphologic changes in the brain observed postmortem are insufficient to explain the symptomatology and signs of hemiplegia. Localized pressure changes, edema, vascular spasm, and thrombosis are factors responsible for temporary damages in bodily functions. Clinical behavior of certain patients, as well as recent observations in man, indicate that the minute vessels of the brain are capable of changing their lumen considerably when under the effect of chemical substances.

The physiologic and morphologic state of the *arterioles* and their relation to the *systemic arterial blood-pressure* are of fundamental importance in determining the rate of the cerebral circulation. A disproportion between the state of the arterioles and the arterial blood-pressure is probably responsible for a number of transient and permanent neurologic symptoms and signs in patients with arterial hypertension.

The preventive measures and therapeutic management of hemiplegias have been presented.

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SECOND MEDICAL SERVICE, BOSTON CITY HOSPITAL

NEPHROSIS

Introductory.—In this country interest in the disease known as nephrosis began with the publication of Epstein's original papers between the years 1912 and 1917.[1, 2, 3] The term "nephrosis," however, is not original with Epstein. Friedrich von Müller[4] in 1905 originally used the term to designate a group of kidney diseases with primary tubular degeneration as distinguished from the evident inflammatory type of kidney lesion. In 1915 Munk[5] proposed the term "lipoid nephrosis" to describe a kidney condition associated with the presence of doubly refractile lipoid bodies in the urine. Finally, in the clinical pathologic classification of Volhard and Fahr[6] we find grouped under the term "nephrosis" those cases having edema as their outstanding feature, with absence of hypertension, retinitis, hematuria, and anemia. In general it may be said that prior to Epstein's communication the term "nephrosis" was synonymous with the type of kidney lesion spoken of as subacute nephritis, chronic parenchymatous nephritis, and chronic nephritis with edema. Epstein demonstrated that nephrosis is not primarily a kidney lesion, but a metabolic disorder with an associated tubular degeneration in the kidneys. That a glomerular nephritis can coexist with this disease has been the belief of most observers. In other words, the case of so-called pure nephrosis is one in which we have a metabolic disorder associated in its later stages with tubular degeneration; the so-called mixed case is one in which, superimposed on this picture, there is a glomerular nephritis. This conception is the basis of many divergent views regarding the etiology of nephrosis and will be discussed later.

Definition.—The following is a brief summary of Epstein's most recent description of the disease.[7]

1. *Albuminuria.*—This is the first sign and may precede other findings by a long period of time. The albuminuria is not due to kidney pathology, but represents an active elimination of serum protein through the kidneys. Due to some fundamental metabolic disorder the serum protein cannot be utilized and is, therefore, excreted. The situation is not unlike that of diabetes mellitus where unoxidized carbohydrate is excreted, giving rise to glycosuria. Hence the descriptive term "diabetes albuminuricus" as applied to nephrosis.

2. *Other Urinary Findings.*—Hyaline and granular casts are often found in large numbers, but erythrocytes are characteristically absent. Also, in most cases doubly refractile lipoid bodies are present. These findings have served to classify the condition as a degenerative disease.

3. *Blood Changes.*—There is a diminution in the amount of blood protein due to the large amounts of protein lost in the urine, which may vary from 5 to 50 gm. daily. Also there is an inversion of the normal albumin-globulin ratio. The globulin content is definitely increased; a change due, probably, to tissue disintegration. In addition to changes in the amount and composition of the blood protein there is an increase in the blood lipoids. This is a constant and characteristic finding in the disease. Cases have been reported with a blood cholesterol as high as 1.3 gm. per 100 c.c. Finally, in the uncomplicated cases there is no rise in the residual blood nitrogen. However, in cases complicated by glomerular damage, there may be a terminal rise in the residual blood nitrogen.

4. *Edema.*—This is the most striking physical finding and is generally the first abnormality noted by the patient. According to Epstein's theory, the edema is due entirely to extrarenal factors and comes directly as a result of the lowered blood protein resulting from the albuminuria.

5. *Basal Metabolism.*—One of the most interesting characteristics of nephrosis is the associated drop in the basal metabolic reading, a finding noted by most observers. It is Epstein's

belief that despite the low metabolism there is no pathologic change in the thyroid gland and no diminution in thyroid secretion, but due to fundamental changes in cellular metabolism, thyroid secretion loses its stimulating effect. In other words there is not enough thyroid secreted to overcome the existing disturbance, and as a result we have a condition of apparent hypothyroidism. Other workers, notably Murphy and Warfield[8] and van den Bergh,[9] suggest that the lowered metabolic reading is only apparent and is due to the inability to properly calculate the metabolic rate because of the edema. Support is given to this explanation owing to the fact that in nephrosis the metabolic reading tends to return to normal as the edema disappears. However, in the case presented below, even after allowing for the edema in the calculation, the metabolic readings were below normal.

Etiology.—Previous mention has been made of the fact that practically all of the earlier writers considered nephrosis a part of the general picture of kidney disease. Munk, in addition to emphasizing the lipoid degeneration, considered syphilis as an etiologic factor. Epstein believes that the disease is a definite clinical entity of unknown etiology, and that it often follows infections, and not infrequently appears during or after pregnancy. Although primarily metabolic in origin, with an associated degenerative tubular lesion in the kidney, there may be a complicating glomerular lesion, inflammatory in nature. In fact, the so-called mixed cases are probably the rule rather than the exception. On the strength of the above conception Epstein explains the so-called amyloid nephrosis and the nephrosis of pregnancy.

It is of interest, however, that not every writer following Epstein agrees with his conception of the disease. For example, Elwyn[10] believes that the condition is due to kidney infection, primarily glomerular. He quotes Stoltz as having found Gram-positive diplococci in the walls of the glomerular capillaries and in the cells of the tubular and intertubular capillaries and cites this as an explanation of the frequency of pneumococcus infections observed by many authors in the course of the disease.

Finally, in support of Epstein's theory, we have at least two outstanding cases of pure nephrosis carefully studied and reported, the one by Murphy and Warfield[8] showing no evidence of any glomerular involvement, acute or chronic at postmortem, and the other, a case quoted by Epstein from Jungmann[11] of pure nephrosis with no anatomic basis on biopsy of the kidney during the acute stage of the disease, and later, at autopsy, showing the typical picture of nephrosis.

In the opinion of the writers the question of etiology is as yet unsettled. This feeling is undoubtedly due to the fact that in this particular locality we see no cases in adults typical of the disease as described by Epstein. We do see cases with undoubted nephrotic elements, but the absence of the so-called pure type from our clinical material does not enable us to state any definite opinions as to etiology.

Treatment.—If we accept Epstein's conception of the disease, then the treatment may be outlined briefly as follows:

1. Replace the loss of blood protein with a protein rich diet as high as 2 to 3 gm. per kilogram body weight.

2. Reduce lipoidemia with a low fat diet.

3. Re-establish normal metabolism and bring about the utilization of protein by administering thyroid.

In the opinion of Epstein, such a course of treatment will result in a complete cure in the uncomplicated cases, although it may require from six months to a year or more.

Frequently, however, treatment is not as simple as indicated above. Due to the complication of glomerular nephritis and the tendency toward azotemia, it may be impossible to prescribe a high protein diet. In such cases other methods must be tried to get rid of edema. Epstein suggests removal of the subcutaneous edema or serous fluids by puncture. Other writers have suggested various diuretics such as salyrgan,[12] novasurol,[13, 14] theophyllin,[15] calcium,[16] and acid-forming salts.[13] Often it is impossible to control the situation regardless of the method of treatment, and the patient succumbs to an intercurrent infection or to azotemia.

It is obvious that no one case can satisfactorily illustrate all

the points of controversy as well as the effects of all the various therapeutic agents recommended for use in this disease. We have chosen, for the purpose of this clinic, 2 cases—one now under observation on our wards and the other a case that died on our service recently. Each of these cases brings out rather strikingly a number of interesting features, especially as regards the etiology of this condition.

Case I.—A. B., a thirty-nine-year-old male, colored, single Portuguese hod-carrier was admitted to the Second Medical Service of the Boston City Hospital, October 17, 1928, complaining of swelling of the legs and abdomen.

His father, mother, a brother, and sister died in Portugal, all of the same kind of "fever." Four other brothers and sisters are living and well. The family history is otherwise negative.

He has had none of the usual childhood diseases and states that he has never been ill before. There have been rare parietal headaches. As far back as he can remember he has had to urinate five or six times a day and three or four times each night. Small amounts of alcoholic beverages have been taken occasionally, but never constantly or in large amounts. His dietary has been varied and contained rather large amounts of meat, fish, eggs, and other protein foods. His average weight in the past ten years has been about 200 pounds.

On July 7, 1927 he appeared in the Medical Out-patient Clinic of this hospital with a primary luetic lesion of four weeks' duration. General physical examination at this time showed the penile lesion and palpable inguinal and epitrochlear glands but was otherwise negative. His urine on that day had a specific gravity of 1.022, a very slight trace of albumin, but no cells or casts in the sediment. The next day it showed the same specific gravity, no albumin, the sediment showed two to three leukocytes, a rare erythrocyte and no casts. The blood Wassermann and Kahn were both strongly positive on July 9th and again on July 13th. He was referred to the Skin Clinic where he received arsphenamin injections during the next three weeks. He then failed to reappear at that clinic until October 2, 1928. On that day he was given 0.3 gm. arsphenamin, and on the 4th, 0.4 gm. His next visit was on the 16th, at which time it was observed that he had marked generalized edema. No further treatment was given, but the patient was advised to enter the Hospital and was admitted the following day.

He had first noticed the edema early in September, 1928. It began in his legs and was intermittent for a few days but soon remained and progressed upward, involving, in turn, the thighs, scrotum, abdomen, arms, and face. Two weeks after the onset he noticed for the first time dyspnea on climbing stairs. This symptom persisted to the time of his entry. He also observed that he had to urinate less frequently and passed smaller amounts, and this became even more marked when, of his own accord, he reduced his fluid intake owing to the increasing size of his abdomen. He had occasional pains in his right lower abdomen when he shifted over on that side.

For two weeks preceding his entry it became difficult for him to get around so that he stayed in bed off and on during this period. There were no other systemic symptoms.

The entrance physical examination showed a well developed and nourished man lying comfortably in bed without dyspnea or orthopnea. His face was puffy, slightly more on the left side than on the right. There was marked pitting edema of the skin over the trunk and extremities, definitely accentuated in the dependent portions. Over the back there was a pigmented macular eruption. Percussion of the lungs and of the heart borders was unsatisfactory because of edema of the chest wall, but there was evidence of fluid in the left chest to the fifth rib and also a small amount in the right chest and probably in the pericardium. A few scattered crepitant râles were heard in both midbacks. The heart sounds were distant but regular. The radial, brachial, and temporal arteries were not thickened. The pulses were equal and of fair quality. The blood-pressure was 140 systolic and 110 diastolic. The abdominal wall showed pitting edema and a fluid-wave with shifting dulness was elicited. The scrotum was enlarged to the size of a large grapefruit and pitted on pressure. He weighed 219 pounds. There were a number of carious teeth and marked pyorrhea. The examination was otherwise negative.

The blood findings at or about the time of entry were: Hemoglobin 70 (Talqvist), red blood-cells 5,090,000, white blood-cells 8500 with a normal smear and differential count. Non-protein nitrogen 30 mg., chlorids 597 mg., plasma proteins 5.32 gm., cholesterol 535 mg., and calcium 8.5 mg. per 100 c.c. The icterus index was 7. The Kahn was negative, the Wassermann anticomplementary.

The urine was yellow, acid, had a specific gravity of 1.022, a very heavy trace of albumin, no sugar, the sediment was loaded with hyaline and granular casts, contained two to three leukocytes to the high-power field, an occasional epithelial cell, and no red blood-cells.

x-Ray of the chest showed "general cloudiness of both lung fields, especially the left base (edema)." The basal metabolism was minus 33.7 per cent. with a pulse of 58 (November 3d).

He was given a Karell diet for the first six days and received 60 gm. of ammonium chlorid daily. After the sixth day, excepting the four days between October 30th and November 2d when he received 120 gm. of protein, he was on a diet with 20 gm. of protein. The ammonium chlorid was discontinued on November 2d. Between October 3d and November 5th he took 1 ounce of Epsom salt daily. For three weeks, beginning November 22d, he received liver extract No. 343 (Lilly)—an extract proved to be potent in pernicious anemia. When this was discontinued, the patient was given 100 gm. of whole liver and this was increased to 150 gm. on January 12th. The protein (other than liver) was raised to 60 gm. on December 26th. Between December 26th and 29th the patient had an acute upper respiratory infection and was given aspirin. There was no other medication administered.

The outstanding feature in the clinical course of this patient during his stay in the hospital was the constant loss of weight at a fairly uniform rate, averaging 1 pound daily regardless of the changes in the treatment. The

edema cleared up gradually but steadily, and the weight has remained fairly constant at 152 or 153 pounds since December 19th. The striking loss of weight under treatment is shown graphically in Fig. 18.

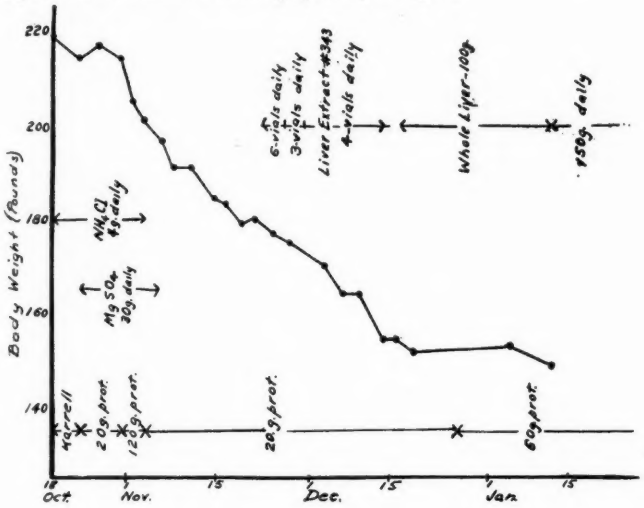

Fig. 18.

The laboratory findings—urine, blood, basal metabolism. The results of the various laboratory tests are noted in Tables 1, 2. The interesting features of the urine may be summarized as follows:

TABLE 1

CONDENSED TABLE OF WATER METABOLISM

Dates.	Average daily intake.	Average daily output.	Specific gravity.	Albumin.	Chlorid.[1]		Sediment.
					Av. per cent.	Av. daily total (gm.).	
10/17–10/22	800	650	1018–1022	4+			Many hyal. and gran. casts. 2–3 w.b.c.,
10/23–10/29	1600	1040	1015–1024	3+, 4+			No r. b. c.
10/30–11/ 2	1575	1375	1012–1020	3+, 4+	.84	11.5	Same.
11/ 3–11/11	1820	1840	1003–1010	3+, 4+	.58	7.7	Occ. hyal, cast.
11/12–11/21	1380	2060	1002–1010	2+, 3+	.48	9.9	Rare gran. casts and w.b.c.
11/21–11/28	2320	2310	1003–1006	2+, 3+	.58	13.4	Rare gran. casts and w.b.c.
11/29–12/ 5	1700	2000	1004–1010	2+, 3+	.58	11.6	Negative.
12/ 6–12/13	1280	1900	1004–1010	2+, 3+	.55	10.5	Negative.
12/14–12/18	1280	1500	1005–1006	3+	.44	6.6	Negative.
12/19–12/25	1300	1400	1005–1006	3+	.33	4.6	Negative.
12/26–12/31	1200	1250	1004–1006	3+	.40	5.0	Negative.
1/ 1– 1/10	1900	2150	1004–1006	3+, 4+	.33	7.1	Negative.

[1] The intake of sodium chlorid was 1 to 1.25 grams daily throughout.

TABLE 2

BLOOD

Date.	Wt. lbs.	Pressure.		Chemistry.					Hgb.[1] Newcomber.	Hematocrit.	R.B.C.
		Sys.	Dias.	Total prot.	Cholesterol.	Calcium.	Chlorid.	N.P.N.			
10/17/28	219	140	110					30			5,090,000
10/22	214	140	115	5.32	535		597				
10/28	215	145	110		535						
10/31	208	155	110		538	8.5		44		32.3	
11/ 8	191	135	110		625	14.1		32		31.2	
11/16	183	130	110		646					33.3	
11/22	180	125	95		614					30.9	6,000,000
11/26	176	130	100		534				83	41.6	5,900,000
12/ 4	170	130	90		375			30		31.4	
12/13	154	110	90		604				78	41.6	5,230,000
12/19	152				535				66	30.6	4,970,000
12/24	153	100	68	4.28	595				63	31.3	4,500,000
1/ 2/29	153			4.05	750			42.5	60	31.3	4,090,000
1/15	147	100	70			12.0	630	30			
Blood-sugar 102 mgm.											

[1] The earlier hemoglobin readings were made by the Talqvist scale and are not included because they are inaccurate.

1. The finding of one urine free of albumin and one showing only a very small amount with no casts but with a small number of red and white cells fifteen months before the onset of edema.

2. The persistent marked albuminuria during the regression of the edema and during the absence of edema.

3. The excess of the output over the intake indicating, of course, loss of edema.

4. The progressive decline in specific gravity in the twenty-four hourly specimens.

5. The rapid reduction in the number of casts, only rare casts having been found after the fourth week in the hospital.

6. The finding of only a negligible number of blood-cells and these only in the first few days.

7. The high chlorid concentration which dropped after the edema had disappeared.

The blood findings may be summarized as follows:

1. No retention of non-protein nitrogen.

2. A transient rise in the blood calcium.

3. A constant high cholesterol level. The only appreciable drop occurred toward the end of the liver extract feeding. On the other hand, there was a return to the high level before the liver extract was discontinued and the highest value occurred during the administration of whole liver. More interesting, however, is the maintenance of the high level during the complete absence of edema.

4. An actual lowering of the total plasma protein in spite of the complete absence of edema. It is interesting to note that there is no edema present, though the total protein is below the "critical level" (5 gm. per 100 c.c.) referred to by Epstein, there being no cardiac or vascular disease demonstrable.

5. A moderate anemia developed during clinical improvement and in spite of liver extract and whole liver feeding.

6. The presence of a positive Kahn and Wassermann before antiluetic treatment and the negative Kahn and Wassermann in the hospital. The first two Wassermanns were "anticomplementary," but the last two were definitely negative.

The blood-pressure showed a definitely elevated diastolic pressure which came down to normal during the decline of the edema and with the patient up and around.

The low basal metabolic rate gradually returned to normal with the regression of the edema. It has been noted that the patient received no thyroid medication. Calculated on the basis of the lowest body weight (70 kg.), that is, if we exclude the edema from the weight used in calculating the basal metabolic rate, his metabolism has been below the lower limit of normal until his edema almost entirely disappeared. This apparently refutes the opinion held by some that the low metabolism is the result of not allowing for the edema in calculating the basal metabolic rate. However, it does not take into consideration the possible influence of the edema on the metabolism of individual cells.

BASAL METABOLISM AND CORRECTION FOR EDEMA

Date.	Pulse.	Weight (kg.).	B.M.R.	B.M.R. corrected (calculated for weight of 70 kg.).
November 3d.....	58	91.5	−33.1	−21.2
November 15th.....	58	81.9	−31.3	−22.1
December 10th.....	58	75.0	−15.6	−14.3
December 16th.....	60	69.3	+ 3.5	+ 3.5
January 11th.....	60	67.3	− 2.9	− 2.9

Discussion.—The clinical picture here presented may be summarized as follows:

A. Insidious onset.
B. Generalized edema with serous effusion.
C. Oliguria.
D. Marked persistent albuminuria.
E. Hyaline and granular casts without hematuria.
F. Absence of demonstrable cardiac insufficiency.
G. Absence of retinitis.
H. Low basal metabolism.
I. Hypercholesteremia.
J. Low total plasma protein.

These findings fit into the clinical picture described by Munk and named by him, "lipoid nephrosis." It is to be noted that doubly refractile lipoid bodies were not looked for, but

Murphy[17] has shown that these are not specific for the pure lipoid nephrosis and he has demonstrated them in cases of chronic glomerular nephritis with marked hypertension and edema. Furthermore, van den Bergh[9] has recently reported a case of pure nephrosis in which these bodies were not found in the sediment, and Epstein has pointed out that they may be considered only as evidence of an advanced lesion.

The question now arises: Is the case presented above one of pure nephrosis or one complicated by a glomerular nephritis? We are inclined to favor the latter idea, because of (1) a history of nocturia of long standing, (2) the finding of a slight trace of albumin and a few blood-cells in the urinary sediment in the Out-patient Department, (3) the raised diastolic blood-pressure on entrance, and (4) the development of a moderate anemia during the edema-free stage.

As to the etiology in this case, three possibilities suggest themselves: Syphilis, chronic infection, and a pre-existing glomerular nephritis. Syphilis seems unlikely in view of the fact that with the onset of edema the patient's blood serology was already negative. Absolutely the only evidence of chronic infection from history or physical findings is a marked pyorrhea. While the chronic sepsis mentioned cannot be ruled out, the far more likely etiologic factor is glomerular nephritis. This would coincide with Elwyn's idea of the pathogenesis of this disease.

Treatment.—It is evident that we did not follow the ordinary treatment with high protein diet and thyroid administration in this case. The patient did receive 120 gm. of protein for three days. He received no thyroid because we were interested to observe what would happen to his metabolism without thyroid medication. The only consistent treatment was a low salt diet and moderate restriction in fluids.

Our chief reason for departing from the usual routine mentioned above was to utilize this patient for an experiment with liver feeding, suggested by Dr. Lindh-Müller of the Thorndike Memorial Laboratory, to whom we are indebted for a large part of the blood work. Pursuing Muelengracht's[18] observation that

in pernicious anemia there is always edema during the advanced stages of the disease, and that a remission can be postulated by an increase in the volume of the urine output, it appears that the water retention may be due to some change in the reticulo-endothelial system and that possibly the same mechanism was at fault in nephrosis. Grossman[19] has recently reported good results from whole liver feeding in lipoid nephrosis. He has also kept his patients on a low salt diet. Lindh-Müller has also studied the cholesterol metabolism in pernicious anemia with liver feeding. Consequently, we were interested to observe the effect of treatment with liver on both the water metabolism and the fat metabolism in this case. It will be noted from the tables that no definite conclusions can be drawn. The fact of the matter is that the patient continued to improve regardless of the nature of the treatment.

It is obvious, however, that this patient is not cured of his disease. He is symptom free and has no demonstrable edema, but the fundamental constitutional changes are still present and active. The albuminuria is still intense and the hypercholesteremia persists. Hence, what we have thus far accomplished is the reduction of the edema and the elimination of the retained salt. This can undoubtedly be ascribed to the low salt content of the diet. Whether with further feeding of liver in larger doses, or with a high protein diet without liver—with or without thyroid administration—we shall succeed in eliminating the albuminuria and reducing the blood cholesterol level to normal, remains to be seen.

Case II.—M. G. (Hospital No. 553118), a twenty-year-old, single, white male Lithuanian bookkeeper, was first admitted to the Second Medical Service of the Boston City Hospital, October 10, 1927, complaining of "swelling of his face and legs." He was apparently enjoying excellent health and was engaged in vigorous exercise at a boys' camp during the early part of the previous summer, until one day in the first week of August, when he had a spell of nausea, vomiting, and diarrhea without apparent rise in temperature. He recovered completely within a day. This is the only known possible infection for a number of years preceding the onset of his edema. One week after this gastro-intestinal upset, and without any other concomitant symptom, he first noticed swelling of his ankles, gradually increasing and extending up his legs. He paid very little attention to this and continued with his usual

exercise. The edema apparently disappeared, but reappeared early in September, when for the first time he observed puffiness of his face and eyelids and edema of the buttocks and genitals. He had no noticeable diminution of his urinary output. His usual weight was 161 pounds and he gained 20 pounds in one month. He consulted his local physician, who found albumin in his urine and advised hospitalization.

Habits.—He used neither tobacco nor alcohol, but his dietary history is of interest because of his high protein intake. He has long been in the habit of eating about a pound of meat, two eggs, and liberal servings of beans and peas, daily.

Family History.—His father is said to have had some kidney disease and died at fifty-six of "ulcers of either the kidneys or stomach."

Past History.—He had had measles, scarlet fever, diphtheria, and pertussis in childhood without complications in any instant. In infancy he had "double pneumonia" and for the past four or five years has had mild attacks of pleuritic pain about every six months. At fourteen years he had a tonsillectomy following a "running ear" of one week's duration. He had had only one head cold in five years. At the age of ten to eleven he had enuresis of unknown cause for about one year. He denied any venereal infection.

Physical Examination.—The patient was well developed and nourished, rather pale, and "pasty looking." His face and lids puffy. His heart was not enlarged and was otherwise normal. The blood-pressure (on entry) was 170 systolic and 80 diastolic. His lungs were clear. There was no demonstrable ascites. The abdominal wall showed moderate pitting edema and the scrotum was enlarged to about four times its normal size. There was moderate edema of the entire lower extremities and of the hands.

Laboratory Findings.—The blood on entry showed hemoglobin 60 (Talqvist), red blood count 4,820,000, white blood count 8100, and a normal differential count. The non-protein nitrogen was 37 mg. per 100 c.c. and the total plasma protein (refractometer method) 5.7 gm. per 100 c.c. The Kahn reaction was negative.

The admission urine had a specific gravity of 1.012, a heavy trace of albumin and no sugar. The sediment contained rare hyaline and granular casts and 30 to 40 leukocytes to the high power field, but no erythrocytes. The phenolsulphonephthalein output on October 15th was 60 per cent. in two hours and ten minutes. The two-hour renal test (Mosenthal) on October 14th to 15th is recorded as follows:

Time.	8–10 A. M.	10–12.	12–2 P. M.	2–4.	4–6.	6–8.	8 P. M.–8 A. M.
Amount.....	160	330	200	390	200	160	640
Specific gravity...	1013	1008	1008	1010	1012	1011	1015

An excess of the output (2080 c.c.) over intake (2000 c.c.) suggested a loss of edema, the nocturia and definite tendency to fixation of specific gravity being evidence of probable chronic renal impairment.

Course.—He was given a diet with 40 gm. of protein, about 1 gm. of salt, and fluids limited to 1500 c.c. The blood-pressure dropped to 155 systolic and 85 diastolic the morning after his entry, and later to 132 systolic and 70 diastolic, at which level it remained. His urinary output was in excess of

his intake, but showed consistently large amounts of albumin, leukocytes 2 to 25 to the high-power field, and hyaline and granular casts, but no erythrocytes. After ten days in bed his edema cleared up entirely. The patient was up and about on the ward and was discharged to the nephritic Outpatient Clinic on November 8, 1927, weighing 160 pounds, with a phenolsulphonephthalein output of 55 per cent.

At home he stayed on a diet containing about 60 gm. of protein, with limited salt and fluid intake. Though he did no work, his edema soon reappeared, his weight rose from 160 to 194 pounds, and for the first time he noticed dyspnea on climbing stairs and diminished urinary output, but no other symptoms.

He re-entered the hospital December 28, 1927. At this time he had marked edema of the lower abdominal wall, scrotum, lower back, iliac crests, and upper thighs. The edema of the feet was only slight. His blood-pressure at the time of this entry was 170 systolic and 80 diastolic, dropping to 155 systolic and 85 diastolic the next morning. The urinary picture was the same as at the previous entry, no erythrocytes being found. The blood hemoglobin was 65 (Talqvist), white blood-count 11,900, red blood-count 3,960,000. Non-protein nitrogen 50 mg. per 100 c.c

For the first three days after his second entry he was given a Karell diet, resulting in a loss of 6 pounds in weight. He was then put on a diet containing 40 gm. of protein, 1 gm. of salt, and 1500 c.c. of fluids. The edema shifted very strikingly, becoming concentrated around his lower back and abdominal wall, upper thighs, and scrotum. His face showed a marked asymmetry after he slept on his side, due to edema of the lower side. His two-hour renal test (Mosenthal) on January 10th was:

Time.	8–10 A. M.	10–12.	12–2 P. M.	2–4.	4–6.	6–8.	8 P. M.–8 A. M.
Volume.....	120	130	105	100	96	115	525
Specific gravity....	1015	1017	1020	1020	1016	1017	1015

Showing a more marked tendency to fixation of amount and specific gravity; this with the definite nocturia and the evidence of retention (1190 c.c. output as compared with intake of 2000 c.c.) was evidence of a definite advancement of the renal involvement.

His basal metabolic rate on January 11th was minus 18 per cent. He was started on thyroid extract (Burroughs and Welcome), $\frac{1}{4}$ grain three times a day. His urinary output averaged about 1500 c.c. There was a consistently large amount of albumin with hyaline and granular casts and many leukocytes and rare to 20 erythrocytes per high power field in the centrifuged specimen. His blood calcium was 11 mg. per 100 c.c. on January 31st. On February 1st the protein in his diet was raised to 80 gm. daily. His edema had cleared up considerably, only a moderate amount remaining in the upper thigh and scrotum. He was permitted to sit up in a chair and showed slight dyspnea on getting out of bed.

At about this time he began to show a series of infectious processes beginning with a furuncle on his right leg. This apparently cleared up, when on February 8th he had a severe chill with a rapid rise in temperature to 103° F. and pulse to 120 and respirations to 28. His leukocyte count rose to 20,000.

The following morning he was markedly dyspneic and moderately cyanotic, respirations were shallow, temperature reached 104° F., and definite signs of consolidation appeared at the right lower lobe. On the 10th he had a second chill, his temperature remained about the same, but some involvement of the left lower lobe was made out. *x*-Ray on the 12th showed pneumonia of both lower lobes, but his temperature, pulse, and respirations promptly began to drop and were normal on that day and remained so. Coincident with this his chest signs began to clear up rapidly and no residual could be demonstrated on the 15th.

The patient took very little food during his febrile period, and on resuming his 80-gm. protein diet he did not tolerate it well. His first furuncle had cleared, but others appeared in succession on his thighs and buttocks. The edema remained stationary during this time.

On February 8th, preceding his pneumonia symptoms, his blood fatty acids were 598 mg. per 100 c.c., the cholesterol, 480 mg. per 100 c.c. His blood-culture showed no growth. On February 17th the edema was on the increase, his blood fatty acids were 556, cholesterol 260, lecithin 240. The blood-pressure was 144 systolic and 86 diastolic. There was no improvement in the edema, but otherwise no change until March 11th, when he again had a chill and rise in temperature, this time due to a septic throat and laryngitis. The temperature ranged from 100° to 102° F. for about ten days, and then again returned to normal and the throat condition cleared up. He had marked hoarseness but no cough. On March 20th he began to have a severe and troublesome diarrhea of ten to twelve movements daily. His appetite failed markedly, his edema was increasing, and for the first time fluid was demonstrated in the right pleural cavity and in the abdomen. He again began to run a low-grade temperature, and on the 26th evidence of a bronchopneumonia in the left base was demonstrated on physical examination and by *x*-ray. He again had several chills, his urinary output diminished, he became drowsy and then stuporous. His blood-pressure dropped to 128 systolic and 70 diastolic. His leukocyte count rose to 56,000 and stayed at that level. His red blood count had dropped slightly below 3,000,000. His non-protein nitrogen rose to 75 on the 24th and then to 120 on March 2d. On March 26th his blood cholesterol was 139, fatty acids 476, lecithin 240. On April 2d a dirty gray membrane was seen on his tonsillar fossa and posterior pharyngeal wall, which showed on culture Klebs-Löffler bacillus and many colonies of hemolytic streptococci. He soon became stuporous and died on April 3d. Permission for autopsy was denied.

The points of greatest interest in this case are the following:

Discussion.—The history, physical and laboratory findings in this case are consistent with a diagnosis of nephrosis with a complicating glomerular nephritis.

1. The definite history of a high protein intake (at least 140 gm. daily) for many years, and development of the edema while on such diet.

2. The absence of demonstrable change in the urinary picture with changes in the edema.

3. The striking demonstration of the susceptibility of these patients to infections of various kinds.

4. The terminal picture of uremia associated with an infection, the drop in blood-pressure, and the marked drop in blood cholesterol without any appreciable change in the fatty acid and lecithin or in the edema.

Summary.—1. Two cases of lipoid nephrosis are presented, each illustrating some of the striking aspects of this disease.

2. In Case I the edema was entirely eliminated by use of a low salt diet. Liver feeding has, as yet, not shown any demonstrable effect on the cholesteremia and albuminuria.

3. Case II represents a patient developing edema while on a constant high protein diet. He also illustrates the marked susceptibility of these patients to infections.

4. Case I tends to support Elwyn's idea of the pathogenesis of lipoid nephrosis. It also tends to disprove Epstein's theory of the relation between edema and the level of plasma protein, inasmuch as the plasma protein level was lowest after the edema had disappeared.[20]

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TWO CASES WITH PURPURA

I WISH to bring to your attention this morning 2 cases presenting the symptom of purpura. You[1] are, of course, all familiar with purpura as a symptom. It is what the laity speaks of as black and blue spots and pathologically represents an extravasation of blood into the skin and mucous membranes. As we shall see later there are various factors responsible for purpura and its significance depends largely, therefore, upon its etiology. In one instance it may be a sign of a very benign condition and in another it may indicate a very malignant disorder. Gradations exist between these extremes.

I have chosen these two patients this morning because they represent widely different types of purpura and thus are to be given very different prognoses.

Case I.—The first patient, Mrs. A. B. S., is perfectly well at the present time. She is at the clinic purely for a follow-up observation. She is a white married woman, twenty-five years of age. She entered the hospital June 15, 1928 with the chief complaint of sore throat and joint pains.

The onset of the soreness of the throat was thirty days prior to her entry. She had a chill on each of two days near the onset of the sore throat. Her gums became sore during the first few days of the disease. There was also some generalized lower abdominal pain which she has continued to have at intervals until her admission to the hospital. Twelve days after the sore throat developed she was seen by her family physician. At this time she had generalized tenderness of the muscles and joints, especially the joints, and, in addition, she showed several purpuric spots scattered over her body. Her temperature was 100° F. At the end of a week in bed, her abdominal pain subsided and she passed two tarry stools. Her right knee became stiff one week before admission and three days later her left ankle became swollen. This joint was not painful, however, until the following day.

There was no previous history of sore throat, but the patient had been

[1] Fourth Year Medical Students.

advised to have tonsillectomy eight years ago. She denied any previous joint pains but stated that she had had frequent "cramps" in her muscles. One year before entry she had an incomplete abortion for which she had a curettage of the uterus. There were no other points of interest in her past history.

Physical examination revealed a slightly obese woman with the following *positive* findings: Her tonsils were large, cryptic, and fibroid without any evidence of exudate or acute inflammation. There were inconstant crepitant râles in the lungs located between the scapulæ and sonorous or sibilant râles over the whole chest. There were a few purpuric areas in the skin of the abdominal wall and some lower abdominal tenderness. The left ankle was red, hot, exquisitely tender, slightly swollen, and painful on motion. Both shoulders were slightly painful on motion but showed nothing objectively.

Laboratory findings on admission: Urine was negative. Phenolsulphonephthalein renal function test, 70 per cent. of the dye excreted in two hours. The red blood-cell count was 4,400,000 per cubic millimeter and the hemoglobin (Sahli) was 86 per cent. The white blood-cell count was 10,000 per cubic millimeter. The blood smear presented no abnormalities. The blood-platelets were present in normal numbers. The blood Wassermann was negative and the blood non-protein nitrogen was 25 mg. per 100 c.c.

Course in the Hospital.—There was rapid improvement in the arthritis following the use of large doses of salicylates (aspirin). Six days after entry there was no redness or swelling of the left ankle but there was still slight pain on motion. At this time one small purpuric area was noted in the skin of the upper right chest. Tonsillectomy was performed thirty-five days after entry without postoperative complications.

The urine remained repeatedly negative. The white blood-cell count remained about 9000 per cubic millimeter. The blood-platelets continued to occur in normal numbers. The bleeding time was normal. The coagulation time of the blood was ten minutes, which by the method used is to be considered normal. The clot retracted well. The stools were repeatedly negative for occult or fresh blood. The patient's temperature was normal or slightly subnormal throughout her stay in the hospital. Her pulse rate occasionally reached 90 per minute but usually was 70 per minute. Her respirations remained from 20 to 24 per minute.

The patient was discharged from the hospital forty-five days after entry and at that time had no symptoms other than asthenia. She has been seen from time to time in the twelve weeks since her discharge. During this period she has had no further joint symptoms but she has continued to show a few purpuric areas in the skin. About eight weeks ago she had some lower abdominal pain and a few days later she experienced a rather severe attack of diarrhea without abdominal cramps, but with considerable mucus in the stools. This disorder responded well to a low residue diet with five feedings a day. She had one profuse menstrual flow about one month after her discharge but no excessive bleeding with her menses since then.

She has gradually returned to her normal health, and appears to be a healthy woman at the present time, as you can see.

Discussion.—The salient points of this case are the acutely painful joints, the purpuric spots, the pain in the abdomen, and the history of the tarry stools. These symptoms and signs are characteristic of the condition spoken of as Henoch's or Schönlein-Henoch's purpura. In establishing a diagnosis in a case presenting purpura one should recognize that there are two idiopathic conditions that present purpura, the outstanding differences between these two being that in one there is a deficiency in the number of the blood-platelets whereas in the other there is no recognizable disorder of the blood itself. The two types may be designated as:

1. Idiopathic purpura (primary purpura), in which there is no blood-platelet deficiency and in which there is no other known pathologic disorder of the blood.

2. Idiopathic thrombopenic (thrombocytopenic) purpura (idiopathic purpura hemorrhagica, morbus maculosus of Werlhof), in which there is a marked deficiency in the number of the blood-platelets.

Idiopathic purpura is generally subdivided into the following types:

1. Simple purpura. In this type there is purpura without other signs or symptoms although urticaria, erythema, and edema are often present.

2. Schönlein's purpura. This is simple purpura associated with painful joints.

3. Henoch's purpura which is characterized by abdominal pain which may or may not be associated with joint symptoms or with purpura. In this condition there may be gastro-intestinal bleeding. It is known that the abdominal pain is due to edema and congestion in some portion of the intestinal tract and cases have been reported in which actual perforation of the intestine has occurred.

In addition to the types of purpura of unknown etiology, *i. e.*, the idiopathic types, there is a large group of conditions in which purpura occurs as a symptom. Symptomatic purpura is directly attributable to some well-known pathologic condition. There are two types of symptomatic purpura.

1. Simple symptomatic purpura. Here there is no known defect in the blood, normal blood-platelets being present in normal numbers and the blood coagulation and bleeding times being unaltered. This is a condition which may occur in endocarditis, venous stasis, epidemic cerebrospinal meningitis, poisoning from certain drugs as quinin and iodids, chronic nephritis, and in many other conditions.

2. Symptomatic purpura with blood defects. These defects manifest themselves by a decrease of blood-platelets (symptomatic thrombopenic purpura) or by an inability of the blood to coagulate in normal fashion as a result of other defects not related to the platelets. In severe jaundice purpura may develop associated with a prolonged blood coagulation time possibly due to unavailable ionized calcium but without any diminution in the number or quality of the blood-platelets. Purpura may arise in association with a diminished fibrinogen content of the blood as sometimes happens in severe hepatic degeneration.

More commonly, symptomatic purpura is found dependent upon a diminished number of blood-platelets. When this is true, the condition is spoken of as symptomatic thrombopenic or thrombocytopenic purpura. Such a disorder may be found in benzol poisoning, aplastic anemia, arsphenamin poisoning, pernicious anemia, the various sorts of leukemias, miliary tuberculosis, and other conditions. As one can readily surmise, the basic cause of the deficiency in the number of platelets may be quite different. For example, in the leukemias there is a displacement of the megakaryocytes by abnormal cells whereas in benzol poisoning there is a depression or destruction of the activity of the megakaryocytes, the cells from which the blood-platelets are thought to be derived.

This somewhat extensive classification and subdivision of the *symptom purpura* may seem confusing to you. The essential points to be remembered are:

1. That purpura may exist either as a symptom of a known disease or as a symptom unassociated with any known disease.

2. That purpura may be due to a recognizable defect in the blood (generally a deficiency in the number of platelets) or it

may be present in individuals who show no blood defects detected by any of the known methods of examination. In other words, we may have symptomatic thrombopenic or non-thrombopenic purpura as well as idiopathic thrombopenic and non-thrombopenic purpura.

It seems logical to believe that some day some of the cases of so-called idiopathic purpura may be shown to be due to some definite diseases or agents. For practical purposes it is only necessary to remember that purpura may be associated with a diminished number of platelets or other causes, which are not so readily demonstrated.

The explanation of the bleeding and the production of purpuric spots in idiopathic purpura, *i. e.*, non-thrombopenic purpura, is not thoroughly understood. The bleeding time and the coagulation time of the blood of these patients are almost always normal. The blood-platelets are always present in approximately normal numbers (as was true in the case described above), and there is no abnormality in the other formed elements of the blood except for slight or, rarely, marked anemia. The blood-platelets are not deficient in thromboplastic material as occurs in hemophilia. The only explanation of the bleeding which seems plausible is that the capillary walls are not normal and thus allow normal blood to escape through them.

Some cases of this condition are associated with diseased tonsils and one of the assumptions is that, in some way, "toxin" is absorbed from them and affects the capillary walls. It will be recalled that this patient had obviously diseased tonsils. A great many cases of idiopathic purpura present transient renal lesions with a urine similar to that found in acute nephritis. It is probable that some sort of toxin affects the kidneys in the same way it probably affects the capillaries of the skin to produce purpura.

The response of this patient to salicylates is worthy of note. It is the response which is characteristically seen in acute rheumatic fever and I do not see how it would be possible to say that this patient did not have acute rheumatic fever as well as purpura of the Schönlein-Henoch type. Certainly the arthritis

was quite like that of acute rheumatic fever since it was wandering in type, acute, readily controlled by salicylates, and associated with infected tonsils. Of course the subsidence of the joints may have been spontaneous and not due to the medication. The joint symptoms of Schönlein's purpura often subside rapidly. The patient has been watched carefully for any signs of rheumatic heart disease since her discharge from the hospital and has shown none.

In connection with the use of salicylates, I should like to call attention to the fact that their use was discontinued after subsidence of the acute arthritic symptoms in order to determine if the arthritic process was still active. No return of the joint symptoms occurred, but salicylates were begun again shortly before tonsillectomy and were continued through the postoperative period. This was done because it is a well-known fact that patients in whom acute rheumatic fever has recently subsided frequently have a recurrence of symptoms following the removal of tonsils, and because this recurrence is not so likely to happen if salicylates are used during the pre- and post-operative periods.

Case II.—Miss O. H. first entered the hospital on October 17, 1928. She was thirty years old, single, with a negative past history except for the following: Tonsillectomy ten years ago; appendectomy six years ago; two teeth extracted in 1927 without any complications.

The present illness began six weeks before entry or about three months ago with a severe head cold, but without sore throat, fever, or headache. On the third day she noticed black and blue spots on both thighs and, within a day or two, similar lesions appeared on the lower legs. No similar spots appeared on the arms until one week before entry when three rather large subcutaneous hemorrhages developed on the left upper arm. There had been no fever. She had had no nosebleed or bleeding from other sources. Her menstruation had been normal until the period four weeks before admission when she had had an excessive flow for two days. On admission menstruation was present. During this menstruation she had increased flow for the first day, but otherwise there was no abnormality in the period. During her illness she had not felt sick and her appetite had been normal. She had eaten a normal well-balanced diet.

The *physical examination* at the time of her first admission was negative except for the following: There was slight oozing along the gum margin about the lower left lateral incisor tooth. There was a small hemorrhagic area on the buccal mucous membrane opposite the right lower molar tooth and a similar but smaller area beneath the tongue. On the left arm there were

several small and large purpuric areas, the largest being approximately 10 cm. in diameter. Both lower legs showed numerous hemorrhages in the skin with small scattered petechiæ on both thighs.

The tourniquet test on the right arm was positive in three minutes. The blood-pressure was 130/80. Pulse 76. Temperature 98.4° F. The bleeding time was five minutes. The blood coagulation time was fifteen minutes which is at the upper limit of normal for the method used. The clot did not retract. Almost no blood-platelets could be seen in a fixed blood smear, or in a fresh preparation stained with brilliant cresyl blue. The hemoglobin was 80 per cent. The red blood-cell count was 3,700,000 per cubic millimeter. The red blood-cells deviated but slightly from normal. The reticulocytes were 1 per cent. The white blood-cell count was 10,000 per cubic millimeter, and the differential count was:

	Per cent.
Polymorphonuclear neutrophils	60
Polymorphonuclear eosinophils	1
Lymphocytes	31
Monocytes	8

The non-protein nitrogen of the blood was 25 mg. per 100 c.c.

The stools were negative for blood.

The basal metabolic rate was −7 per cent.

Five days after admission the blood-platelets counted by Wright's method were 60,000 per cubic millimeter. Four days later they were 140,000 per cubic millimeter. No new hemorrhages occurred in the last four days of her first visit to the hospital. She was discharged from the hospital six weeks ago and requested to rest at home.

Four weeks ago her white blood-cell count was 12,000 per cubic millimeter and the differential count was normal. The red blood-cells were normal. The blood-platelet count was 200,000 per cubic millimeter. She had had two small purpuric areas soon after going home, but none since. She resumed work three weeks ago apparently well.

Today she has been admitted to the hospital again on account of numerous purpuric areas scattered over her body and epistaxis of moderate degree, which occurred yesterday.

Her blood-platelets now number 44,000 per cubic millimeter. The white blood-cell count is 16,000 per cubic millimeter.

Discussion.—This case presents a decidedly different picture from Case I. This patient has purpura which is associated with a deficiency in the number of blood-platelets, an essentially normal blood coagulation time, and a non-retractile blood-clot. These are the characteristic blood findings in thrombopenic purpura. The reason clotting occurs in normal or slightly greater than normal time is because there is thought to be present in each blood-platelet a normal amount of thromboplastic

material. However, the total amount of this material in a unit of blood is small due to the deficient number of platelets. As a result there is sufficient thromboplastic material to initiate blood clothing but an insufficient amount to cause normal clot retraction. In hemophilia there is a different arrangement. Here, there are blood-platelets in abundance, but they are abnormal in quality and hold the thromboplastic material longer than usual and hence the coagulation time is prolonged. However, there is plenty of this material eventually set free and thus a well formed and retractile clot finally occurs. A second finding of interest in thrombopenic purpura is the prolonged bleeding time. This is typical of thrombopenic purpura, perhaps because there is a general deficiency of thromboplastic material and the tissue juice suffers along with the other fluids. Whereas in hemophilia, the tissue has plenty of thromboplastic material and hence the bleeding time is normal.

At the time of this patient's discharge from the hospital I felt that there was a great likelihood that the condition would spontaneously clear up and this opinion was strengthened by the examination made four weeks ago at which time there were 200,000 platelets per cubic millimeter. However, her return to the hospital today with purpura, epistaxis, and a blood-platelet count of 44,000 per cubic millimeter makes me somewhat skeptical as to the outcome. One must be very cautious regarding prognosis now that there has been a recurrence. Recovery is possible but one must be ready to expect an unfavorable progression of her disease. The recurrence simply serves to emphasize the fact that a correct prognosis cannot always be made at the time of a patient's first admission to the hospital with idiopathic thrombopenic purpura.

I recall another patient with thrombopenia whom I saw about two years ago. He had some malaise, a chronically infected maxillary sinus, and had known that he had had eosinophilia some years previously. On examination of a blood smear, the blood-platelets were obviously diminished and this impression was confirmed by a count, which showed them to number 70,000 per cubic millimeter. The sinus infection cleared. The blood-

platelet count gradually rose and the patient made a good recovery. He never showed any purpuric spots but his blood-platelet count was at the point where it could not have dropped much more without their appearance. When the platelets are reduced below 50,000 to 60,000 per cubic millimeter purpura usually appears.

This last patient represents a mild type of thrombopenia. It is a condition which is frequently unrecognized and may clear up spontaneously. Case II represents a type of thrombopenic purpura which is a somewhat more severe condition than the simple thrombopenia just spoken of, but it probably has much the same etiologic basis, *i. e.*, a respiratory infection.

If this second patient does not improve and profuse bleeding occurs it will be necessary to consider transfusions of blood and removal of the spleen. Splenectomy offers excellent chances for relief of symptoms in patients suffering from idiopathic chronic congenital or acquired thrombopenic purpura. However in the more acute types of this sort of disorder splenectomy has yielded much less brilliant results. Deep *x*-ray therapy is a form of treatment to consider but I feel that this can accomplish much less good than splenectomy. In case of emergencies arising from hemorrhages, repeated blood transfusions offer the best chance for the relief of symptoms.

In closing I would like for you to carry away the following points:

1. There are two main types of purpura, viz., that with blood-platelet deficiency and that without platelet deficiency. These may be symptomatic or idiopathic. Schönlein-Henoch's purpura is merely a non-thrombopenic purpura of unknown etiology and without abnormality of the formed elements of the blood.

2. Simple respiratory infections may cause thrombopenic purpura.

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EXPLORATORY LAPAROTOMY IN CASES OF DOUBTFUL ABDOMINAL MALIGNANCY

BOTH the physician and surgeon are not infrequently called upon to decide as to the advisability of exploratory laparotomy in patients strongly suspected of having malignant disease in the abdominal cavity. In some of these cases the evidence for true malignancy is overwhelming and clear cut. In others it may be scant indeed. All cases, however, fall into one of three groups—first those in which the diagnosis is virtually proved. The symptoms presented are those of malignancy, a mass is felt, *x*-ray examination confirms the suspicion and external metastatic nodes may be found suitable for excision which prove on microscopic examination to be malignant. Here there is rarely, if ever, a call for laparotomy unless it be to relieve stasis or obstruction in a comparatively young and robust individual. Secondly, there are cases in which one feels reasonably sure that malignancy is present but actual proof is lacking and lastly cases which might be neoplastic or might be some non-malignant disease. It is in these latter two types of cases that laparotomy is often indicated and probably should be undertaken more often than is the custom. Exploration of the abdomen nowadays, is, in good hands a comparatively safe procedure and the situation often resolves itself into the question of whether the evidence for inoperable malignancy is so clear cut that surgical interference is not justified. If malignancy is present and inoperable nothing further can be done but the mere opening of the abdomen is, as has been said, a comparatively safe procedure, and as a rule no harm results. Some cancerous cases, it is true,

take a definitely downward course after such a procedure, but others may improve markedly. If malignancy is present and operable there is a chance, albeit a small one, for recovery and cure at least over a period of years. If no malignancy is found the condition may be a benign tumor or some other operable condition that can be definitely helped or cured. These latter cases, to be sure, are rare, but not so rare as spontaneous recovery from true malignancy. The hope may be small indeed but the alternative is progression of a tumor to inoperability, change of a benign into a malignant process or persistency with perhaps death from the non-neoplastic disease.

A number of such cases have recently come to my attention and they serve to illustrate the belief that laparotomy for supposed malignancy is often a wise and useful procedure.

Case I.—Dr. X, a middle-aged physician, who had previously enjoyed the best of health, began in the spring to feel abnormally tired and he found it increasingly difficult to do with ease the routine work which had previously been a pleasure. With this abnormal fatiguability he had occasional attacks of diarrhea of no great severity lasting a few days and recurring at frequent intervals. No blood or mucus was noted in the stools and there was no tenesmus or abdominal pain. These symptoms gradually increased over a period of several months with gradual, but slight, loss of weight until he was forced to give up his work entirely and remain in bed. Four months in bed, however, failed to improve his condition. It was found at this time that his red blood-cell count was 1,600,000 per cubic millimeter and his hemoglobin 40 per cent. and white blood-cell count 2400. No symptoms other than abnormal fatigue and occasional attacks of diarrhea were present. The loss of weight was insignificant. The case was diagnosed pernicious anemia by his local doctor and the patient was put upon a liver diet. He immediately began to improve and in a month his red blood-cell count had risen to 4,800,000 per cubic millimeter. He did not actually feel very much better, however—a point incidentally much against the diagnosis pernicious anemia—and he was still unable to do much work or even enjoy himself about the house. A revision of his blood count by a consultant revealed the fact that while his red count was 4,800,000 his hemoglobin was but 50 per cent. and the stained smear showed a preponderance of small achromic cells rather than essentially normal cells. The blood was, therefore, characteristic of secondary rather than primary anemia and in the absence of renal involvement or symptoms pointing to disease of any of the systems it was believed that the anemia was due to internal bleeding. Gastro-intestinal *x*-rays were interpreted as indicating the presence of a tumor of the stomach. Gastric analysis revealed no free hydrochloric acid after test-meal and the stools showed a positive guaiac test. Another *x*-ray taken a month later showed definite increase in

the size of the tumor and laparotomy was advised. At operation an incision into the stomach showed on the anterior wall just above the pylorus a pedunculated tumor the size of a hen's egg partially obstructing the outlet from the stomach. The narrow pedicle was severed by actual cautery and the stomach well closed. Pathologic examination revealed a benign adenoma with no areas of malignant degeneration. A rapid recovery was made and the patient is now, two years later, in perfect health.

Case II.—A. K. A single white woman of fifty-two entered the Boston City Hospital on August 26, 1928. The chief complaint was of loss of appetite and strength for eight months and a gradually increasing pallor over a slightly longer period. In the past she had always been a healthy robust woman. In 1918 she had had influenza and was confined to the house for three weeks, but at no time was she seriously sick. In 1919 she had an uncomplicated attack of appendicitis with appendectomy. Two years before the onset of the present symptoms she weighed 148 pounds. In the last year she had lost nearly 15 pounds and she felt sure that most of the loss occurred during the past seven or eight months. The past history was in other respects normal, and she had had in particular no symptoms referable to the gastro-intestinal tract. Eight months before entry to the hospital she began to notice that her strength was leaving her and that she was gradually growing much paler. Her color had previously been good. Her appetite became almost nil and, in fact, she lived virtually on corn flakes and tea—an important fact if for no other reason than that it might well explain the loss of weight and quite possibly the pallor. These symptoms increased and four months before admission she fainted while at her house work. She had, however, no abdominal pain, nausea, or vomiting. There was no hematemesis, melena, or jaundice. The entire picture was of loss of strength and increasing pallor.

The physical examination on entrance to the hospital showed a pale, rather restless, flabby looking woman of past middle age. The mucous membranes were distinctly pale. No external lymph-nodes could be palpated. No skin lesions were present. The lungs presented no abnormalities. The pulse was 120, regular, and of fair quality. The heart was not enlarged, the sounds were of good quality, and over the mitral area was a soft, late diastolic murmur. No peripheral signs of aortic regurgitation could be made out, but the first sound at the apex was sharp and slightly accentuated. The blood-pressure was 100/80. Through a lax abdominal wall one could palpate in the left upper quadrant an irregular very firm mass about the size of a hen's egg. It was definitely though not markedly tender and descended on deep inspiration several inches below the costal border. No other masses were felt. The extremities were normal and the Wassermann and Kahn were negative. The blood examination showed 2,830,000 red cells, an hemoglobin of 25 per cent., and a white count of 8000. The differential count was essentially normal. Gastric analysis showed no free hydrochloric acid and a strongly positive guaiac in the fasting contents, but a bare trace of hydrochloric acid after the test-meal. The stools, aside from a positive guaiac test, were not abnormal. Gastro-intestinal *x*-rays were interpreted as showing "cancer of the pyloric region of the stomach." Chest plates showed haziness at both

bases, but no definite evidence of metastasis. The evidence for carcinoma of the stomach seemed clear. In the ward she became rapidly worse, the hemoglobin falling to 16 per cent. and the red count to 1,000,000. Her temperature rose—as it often does in internal hemorrhage—and for a week or more fluctuated between 99° and 100.5° F. She was given liver in large amounts daily and a transfusion of 500 c.c. whole blood. The red cell count rose promptly to 4,000,000 and the hemoglobin to 60 per cent. Her general condition also improved markedly, though her appetite remained poor and the mass in the left upper quadrant did not materially change in size or consistency. In spite, however, of the palpable mass and the almost certain diagnosis of carcinoma of the stomach she was transferred to the surgical service and the abdomen opened. A mass somewhat smaller than a hen's egg was found at the pylorus. Careful exploration revealed no involvement of the regional lymph-nodes. Nor was there any infiltration into the surrounding structures. The mass was easily excised and a gastro-enterostomy performed. Pathologic examination (S–28–2554) showed a tumor of the stomach projecting outward rather more than inward. The microscopic diagnosis was endothelioblastoma—a rapidly growing tumor—locally malignant but not, as a rule, metastasizing.

Case III.—R. H., a man of thirty-seven years, entered the hospital on August 29, 1928 with a chief complaint of a lump in the right lower quadrant.

In the past he had been a healthy, hard-working man and had had no illnesses of importance. His gastro-intestinal tract had given no trouble of any sort.

A year before entry he began to be constipated and he found it increasingly necessary to take cathartics. With this constipation he had some "gas pain" in the lower abdomen, never severe enough to stop his work and generally, though not invariably, relieved by proper catharsis. There was no loss of weight or appetite. Six months before entry he himself found a mass in the right lower quadrant which was non-tender and apparently fixed. This mass gradually grew in size. His constipation gave way to moderate diarrhea with four or five stools a day, often watery and on two occasions, according to him, containing blood. He began at this time to lose weight and in the two months preceding his coming to the hospital he had dropped off 15 pounds, though his appetite continued to be fairly good and he did not particularly worry about his condition. After a month of diarrhea his constipation returned and subsequently alternated with short periods of watery diarrhea, not apparently attributable to cathartics.

The physical examination on entrance showed a rather thin man prematurely old, in considerable abdominal discomfort. The temperature ranged, during his two weeks on the medical wards, between 99° and 100° F. Pulse normal. The heart and lungs presented no abnormalities. The abdomen, definitely distended, revealed a mass about 4 inches long in the right lower quadrant. It was movable, though not freely so, and was not tender. From day to day the ease with which it could be felt varied markedly. The rest of the abdomen was distended with gas. On several occasions the patient experienced rather severe cramp-like pains all over the lower abdomen

and at these times the tympanities became more marked and some rigidity and visible peristalsis could be made out. Moderate diarrhea alternated with rather obstinate constipation. The liver edge was just palpable. There was no free or occult blood in the bowel movements. The blood was normal. Gastro-intestinal *x*-rays did not reveal any definite abnormality.

The general consensus of opinion was that the most likely diagnosis was carcinoma of the large intestine, though tuberculosis was considered a possibility. After consultation with the Surgical Staff it was decided to explore the abdomen. At operation a large mass was found at the lower end of the small intestine. A rush diagnosis of carcinoid of the intestine was made and 3 feet of ileum was resected. Subsequent pathologic examination (S–28–2347) confirmed the diagnosis of carcinoid. The loops of intestine excised were drawn together in a knot-like mass. The mesentery was thicker and firmer than normal and multiple sections showed a great increase of scar-like tissue forming coarse bands through and about the gut. Scattered through the interior of the intestine were numerous firm nodules about 2 mm. in diameter. One nodule was 1 cm. in diameter and slightly ulcerated on the surface. There was no invasion of the mesentery by actual tumor tissue. Today three months after operation, the patient has gained 30 pounds and is in every way normal except a slight occasional attack of diarrhea.

Case IV.—M. B., a woman of sixty-eight years, entered the hospital complaining of loss of appetite and gas on the stomach for eight months. During this period she had also had vague epigastric distress and the symptoms had all gradually increased in intensity. There was no real pain, no nausea, vomiting, jaundice, or diarrhea. The epigastric distress during the three weeks prior to entry had become much worse, appearing as a rule after meals, not relieved by soda or by food. There was a loss of weight of 10 pounds during the last two months, no doubt in part due to anorexia.

The past history was entirely irrelevant.

Physical examination showed considerable tenderness in the epigastrium together with a definite sense of resistance but no mass could be felt. The liver and spleen could not be felt. There were no external lymph-nodes palpable. The remainder of the physical examination was normal.

The stools were normal with a negative guaiac test. No abnormalities were found in the blood. The urine was normal. Gastric analysis revealed complete absence of hydrochloric acid but no free blood or other evidence of malignancy. Gastro-intestinal *x*-rays showed a slight filling defect in the region of the antrum and a definite five-hour gastric residue. An *x*-ray diagnosis of carcinoma of the stomach was made.

At operation a polyp 1½ inches long was found in the stomach near the antrum and partially obstructing it. It was removed by actual cautery.

The pathologic examination (S–27–2884) revealed a base of connective-tissue covered with glandular epithelium in places atypical in character and showing fairly numerous mitotic figures. There was no ingression of the base by this epithelium. The tumor was to be regarded with suspicion but owing to the lack of infiltration at the base the prognosis is probably favorable.

Case V.—M. T., an old lady of eighty years, entered the hospital under the care of Dr. E. N. Libby, to whom I am indebted for the opportunity to report the case. She complained on entrance chiefly of a continuous dull pain in the epigastrium and of vomiting over a period of eight months. Except for typhoid fever and malaria in childhood she had had no important illnesses. In fact she had been an unusually strong and vigorous woman all her life. Eight months before entry she developed a severe, dull pain in the epigastrium, nearly continuous and not particularly affected by food or medication. At the same time she became weaker—a not unnatural symptom at eighty years of age. Several weeks before admission she began to vomit, the vomitus consisting largely of undigested food. There was no gross or microscopic blood in the vomitus when she was on the wards but there was considerable mucus. There was no jaundice or melena. No other symptoms of importance were found.

The physical examination showed very extensive arteriosclerosis and feeble heart-sounds. No masses could be felt in the abdomen which showed nothing abnormal except some tenderness and resistance in the upper portion. The urine was negative. In view of the cardiovascular condition and the patient's generally poor condition she was operated under spinal anesthesia. She, however, was unable to stand the shock and died on the table. The autopsy (A–28–389) showed a pedunculated tumor arising from a small stalk not more than 1 cm. in diameter and completely blocking the pylorus. There were no evidences of infiltration or metastases. The microscopic examination showed the base of the tumor consisted of smooth muscle-fibers which are separated owing to edema. There is a marked infiltration with plasma-cells and eosinophils. The surface is covered by glandular epithelium, the cells being columnar and atypical. This epithelium shows many mitotic figures and has in places invaded the muscularis. The peripheral portions of the polyp were covered with normal epithelium. Diagnosis: Gastric polyp not to be regarded as malignant. Complete removal should offer a favorable prognosis.

The first case cited is an excellent example of what may be accomplished for the patient when the diagnosis is distinctly in doubt. Pernicious anemia had been diagnosed on quite unsatisfactory grounds. Secondary anemia in a man of his age and in absence of any signs of renal disease or other pathology is very often due to malignancy. One *x*-ray was interpreted as showing a new growth, another at a different but thoroughly first-class hospital showed none. Laparotomy revealed a completely remediable condition in the shape of a polyp.

The second case was that of an endothelioma of the stomach. The growth of these tumors is usually slow but progressive, and in a certain sense they are, therefore, comparatively benign.

But they are liable to recur and it is therefore wise to excise very widely if they are encountered. What the subsequent history of this case will be it is impossible to say, but at least she has a far better chance than she would have had, had not the operation been done.

The case of carcinoid of the intestine again illustrates the advantage of early operation. These embryonal carcinoid tumors were first described by Lubarsch and are not infrequently found in the small intestine and its mesentery. Excision would seem fully justified.

Polyps of the stomach are not excessively rare. They may give all the signs and symptoms of cancer. Malignant changes have been described and their early and complete removal is wise. Not infrequently, as in the cases described above, a ball valve is formed by them obstructing the outlet from the stomach and rendering the symptoms far more serious than the comparatively benign nature of the process warrants.

In addition to the conditions illustrated above we have leiomyosarcoma of the stomach, characterized as a rule by gross and early gastric hemorrhage. The tumors are, in their early stages, sharply delimited and they metastasize late but widely. If discovered in their early stages their successful removal would seem to offer a good prognosis. Stone in the common duct has been mistaken not infrequently for cancer of the pancreas and the patient allowed to die when operation could have saved him.

As regards actual cancer of the stomach and the advisability of operating on it, much of a pessimistic nature has been said and written. It is undoubtedly true that the vast majority of carcinomas are even when first seen, inoperable. But a case on the Fourth Medical Service recently came to autopsy—death being due to bronchopneumonia—in which a definite diagnosis of cancer of the stomach had been made clinically and which had no metastases locally whatever. The tumor was small and freely movable, no glands were involved and no extension could be found. Certainly here a complete excision might have offered at least a reasonable chance of cure.

Many years ago the late David Cheever said: "Is there a last chance? Is this forlorn hope likely to lead to anything or surely going to lead to death? If the latter, the surgeon is not justified in operating. If there is a chance and the patient clearly understands it, I think myself he is entitled to the benefit of this slight chance if he wants it."

CLINIC OF DR. LEWIS WEBB HILL

CHILDREN'S HOSPITAL

PYLOROSPASM AND CARDIOSPASM IN AN INFANT

THIS child is two years of age and weighs 34 pounds. I think you will all agree that he is in excellent condition, and it is hard to believe there is anything the matter with him. He has the following history:

At birth he weighed 8 pounds, and was an unusually vigorous baby. He was partly breast and partly bottle fed. His chief trouble has been vomiting, which began when he was first fed. This vomiting was after nearly every feeding, and has been occasionally explosive, though ordinarily not so. He had been fed various mixtures of whole milk, Dryco, cream and skimmed milk, all of which were reasonable formulas for his age and weight, without any effect upon his vomiting. He gained weight well for a while, but in the last three weeks has been losing about 2 ounces a week.

I first saw him when he was fifteen weeks of age. He then weighed 13 pounds, 4 ounces, and was in fair nutritional condition. Physical examination at that time was negative except for well-marked visible gastric peristalsis. A diagnosis of pylorospasm was made, and he was taken to the private ward of the Children's Hospital, and was given the following formula

2 per cent. milk	20 oz.
Water	4 oz.
Dextri-maltose No. 1	6 level tablespoonfuls
Farina	3 rounded tablespoonfuls

He stayed in the hospital a week, did not vomit at all during this time, and gained 7 ounces. On January 17th he was discharged, still taking the same feeding, and did very well until about the middle of March, when he began to lose his appetite, so that all his food had to be forced. According to his mother he seemed to have a good deal of distress while eating, and would hold milk in his mouth a long time, although he apparently had no actual difficulty in swallowing. He spit up a good deal, but vomited only occasionally. According to his mother, he "was a very hard baby to feed, and does not like anything." Solid food such as egg-yolk and cereal was begun at about eight months, and by dint of a tremendous amount of exertion his mother, who was a very painstaking woman, was able to keep his nutrition up. July 20th, when he was about ten months old, she brought him to me in despair, saying that she "knew there was something the matter with the baby," and that "it hurt him to eat" and that an *x*-ray must be taken of his stomach

to see if it was normal. At this time the baby weighed 21 pounds, 8 ounces, was not vomiting, had no visible peristalsis, and would have been passed anywhere as a normal baby. More to please the mother than anything else, roentgenograms after a barium meal were taken. The report was as follows:

"Roentgenograms of the esophagus and stomach show either spasm or stenosis of the esophagus near the cardiac end of the stomach. The esophagus is slightly dilated above the constriction. Plenty of barium enters the stomach, and the stomach empties itself normally." So there was apparently a real basis for this baby's difficulty, which shows very well in Fig. 19.

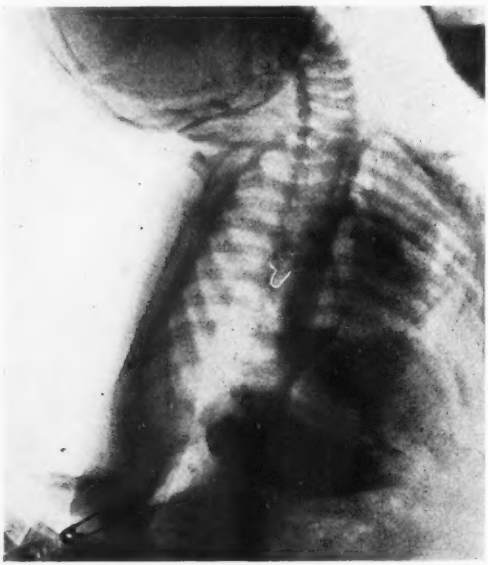

Fig. 19.

He was referred to Dr. H. G. Tobey for esophagoscopy, who found a definite narrowing of the esophagus near its entrance to the stomach. He stated that he could not be sure whether it was organic or of a spasmodic nature. He dilated the esophagus with a No. 18 sound, and the baby was discharged, taking the same diet that he had before he entered the hospital, and was to return later for another dilatation if he did not improve.

He did very well for about three months after his dilatation, but then his symptoms returned, and now (November 10, 1928) it is just as hard to feed him as it was before the dilatation. His mother's statement is as follows: "He takes solid food very poorly, and cannot seem to swallow any food unless it is very finely divided. While eating he says, 'I gag,' and 'I feel sick,' and

the least little thing will start him gagging. He seems to have difficulty in swallowing, but does not often vomit, perhaps four or five times a month. When he does vomit it is sometimes explosive."

Physical examination shows him to be overweight for his age, and in excellent physical condition. There is no visible gastric peristalsis. Roentgenograms after a barium meal were again taken. "There is a slight delay at the lower end of the esophagus, with a slight dilatation of the esophagus. There is no holding up of the meal, however, for any unreasonable time. There is not the dilatation of the esophagus that would be expected if there were a permanent stricture of the lower end."

Discussion.—The interesting thing about this patient is the association of a cardiospasm with an earlier pylorospasm. Pylorospasm is common in young infants, cardiospasm extremely rare in infants, and very rare in children. The fact that the second roentgenogram, taken more than a year after the first, shows no constriction of the esophagus and that the esophagus is not very much dilated, is almost certain evidence that the condition is a functional one entirely.

The diagnosis, by means of the Roentgen ray, is not difficult, if one is suspicious enough of the condition to have plates taken. In this case the cardiospasm was probably not present at the time the pylorospasm was, for the baby did very well for some time after thick cereal had been started. His cardiospasm probably began at about six months, and gave symptoms even while he was taking a liquid diet. Organic stenosis of the esophagus does not manifest itself, unless it is a complete or nearly complete atresia, until the infant begins to take solid food, when it is noticed that milk goes down well, but solid food does not. The point that I wish to bring out is that while cardiospasm is a rare condition in infants, it is worth while to bear it in mind, and to have plates taken if the symptoms warrant it.

Treatment.—Atropin had been tried for this baby, without a great deal of result, but is probably worth while trying again, so we will give him 4 drops of a 1 : 1000 solution of atropin sulphate twenty minutes before each feeding, later increased to 5 drops. This gives him about 1/200 of a grain at a dose. It will be necessary to have all of his food in a finely divided state,

and if he takes milk poorly it will be well to reinforce it with a carbohydrate, such as lactose or dextri-maltose. Olive oil is also useful, and two teaspoonfuls three times a day will add about 250 calories to his diet. As a matter of fact, although it has been difficult to feed this baby, his nutrition has been excellently maintained. This and the rather infrequent vomiting are unusual. The best treatment is dilatation, and this will probably have to be done again.

TUBERCULOSIS OF THE ABDOMINAL LYMPH-NODES

THIS boy is four years of age. He had measles and mumps as a baby, otherwise his past history is negative. He did well as a baby, and there was never any trouble as regards his feeding. He took for a considerable period, while in a neighboring town, a raw milk of somewhat uncertain origin. For the last few months he has been taking pasteurized milk.

He has been sick for twelve days, and his chief complaint is abdominal pain. He vomited at the onset, and usually at least once a day since. He has had no fever, according to his mother, for the last few days, but had some at the onset, degree unknown. His abdominal pain has not been localized, and for the most part has not been very severe except for a period of about two hours two days ago, when it was so bad that he cried with it. His bowels are constipated. His urination is infrequent, and he occasionally has some dysuria.

Physical examination shows him to be rather soft and flabby, and only in fair condition. Nothing of importance is noted, with the exception of the abdomen. This is slightly distended, soft, and non-tender everywhere. About the cecum are felt several small masses, which are apparently enlarged glands. One about the size of a marble is felt in the left lower quadrant. These are freely movable, and tender only to deep pressure. The urine was clear, and showed no albumin or sugar. Mouth temperature was 99.4° F. He was sent to the private word of the Children's Hospital for observation.

The intracutaneous tuberculin test was strongly positive in a dilution of 1 : 1000. A roentgenogram of the abdomen showed a small dense place in the right lower quadrant, which the roentgenologist interpreted as a calcified gland. During his stay in the hospital his temperature was not elevated, and he complained of no abdominal pain. He was discharged at the end of a week with a diagnosis of *tuberculous abdominal lymph-nodes.*

Discussion.—I have selected this case because the child with recurring abdominal pain as the presenting symptom is very common, and it is often difficult to arrive at a correct diagnosis. Such a child is usually not very sick: he complains to his parents that his "stomach hurts him," and he says it so often that they finally pay some attention to him, and take him to a doctor. There may also be more acute attacks, such as in the boy we have been discussing. It is often very difficult to know what is the matter with these children, and in many cases a positive diagnosis cannot be made. There may be no underlying path-

ology, and the cause of the pain may be indigestion. Inquiry into the dietary habits and examination of the stools, particularly for undigested and fermenting starch, should either confirm or rule this out.

If there is any actual pathology it is most likely to be in the appendix or in the abdominal lymph-nodes (tuberculosis). I have seen very few cases of chronic appendicitis, but do not agree with those who deny that it exists. I should be very reluctant to recommend removal of the appendix unless there was very strong evidence that it was at fault. Roentgen-ray examination after a barium meal, while by no means conclusive, is of a good deal of value in making the diagnosis, when taken in conjunction with the clinical symptoms, and the exclusion of other causes for abdominal pain. Delayed emptying of the appendix and, particularly, fixation and tenderness under the fluoroscope are significant findings. While I would by no means ignore chronic appendicitis as a cause of abdominal pain in small children, I believe that it is not a very common one, and that all other causes should be very carefully excluded before operation is performed and, furthermore, that operation should be done only if the pain is frequent enough, and severe enough to cause the child a great deal of trouble. One is too likely to find a normal appendix.

Tuberculosis of the tracheobronchial lymph-nodes is very common in children, and I have a feeling that it is equally common in the abdominal lymph-nodes, although not so frequently recognized. Indeed, in many cases it is not possible to make the diagnosis with certainty, but it should always be suspected in children who have repeated attacks of abdominal pain of moderate degree without any other recognizable cause. Fever and vomiting may or may not be present, the child may be in good general condition, or obviously "run down." It may or may not be possible to palpate the enlarged nodes, and they show in the roentgenogram only if calcified. If the tuberculin (intracutaneous) test is negative, we can almost certainly rule out tuberculosis: if it is positive we cannot accept it as very important evidence, for so many children above the age of two years give

a positive test. It is very difficult to compile any accurate figures for the incidence of the tuberculin test in children, for the reason that those who have reported large groups have worked with such varying types of children, mostly of the hospital class. Some have included obvious cases of tuberculosis, some have not, and so on. Our earlier conception of the tuberculin test was based on the German figures, and there is no question now that these figures are altogether too high for American children. As far as I know, no large series of tuberculin tests have ever been done on healthy school children. This is what is needed in order for us to form a more accurate opinion of its significance. The figures I usually go by are those of Dr. Charles Hendee Smith, from the Bellevue Hospital, New York, reported in 1926.

They are as follows:

	Per cent. positive.
0 to 6 months	4.75
6 to 12 months	9.45
1 to 2 years	9.35
2 to 4 years	14.5
4 to 6 years	16.2
6 to 8 years	30.0
8 to 10 years	29.0
10 to 12 years	42.3
12 to 13 years	45.5

To return now to our patient. He has symptoms, he has been in the habit of drinking raw milk, he has palpable glands, he has a slight elevation of temperature, a positive tuberculin test, and a calcified gland shows in the roentgenogram. We certainly need no more evidence to make a positive diagnosis.

This is a rather positive case: Most are not so. We have in most cases symptoms only, occasionally palpable glands, which, of course, may or may not be tubercular, and only rarely enough calcification to show in the roentgenogram. From the parents' point of view making a diagnosis of any sort of tuberculous infection in a child is a very momentous thing. For this reason these suspected cases of abdominal tuberculosis, where the evidence may be by no means positive, are very difficult to deal

with, and it is not easy to decide whether or not to mention the dread word "tuberculosis" to the parents. With a positive tuberculin test, palpable glands, and symptoms extending over a considerable period of time, a child not in very good general condition, without any other apparent cause, I am inclined to make a positive diagnosis, but am very loath to do it with any less evidence than this, although I may very strongly suspect it.

The infection is of the bovine type in about half the cases, and comes from drinking raw milk from tuberculous cows. A child runs practically no danger of contracting tuberculosis from milk, whether it be raw or pasteurized, if the cows have been tuberculin tested at frequent intervals. As a matter of fact, most tuberculin-positive cows, unless from grossly neglected herds, show at autopsy only very small foci of tuberculosis, and usually in such locations that it would not be possible for bacilli to get into the milk from them. Tuberculosis of the udder is very rare. Tuberculosis of the lung is more common, but by the time a cow had reached this stage she would be in such condition that she would have been taken out of the herd by any ordinarily conscientious herdsman. Raw milk may carry with it other dangers, but proper control of a herd by means of sufficiently frequent tuberculin tests should make it rather improbable for a child to contract tuberculosis from milk.

Prognosis.—Tuberculosis of the abdominal nodes may again be compared to infection of the tracheobronchial nodes, and we know that most of these recover. I feel sure that a great many children have had tuberculosis of the abdominal nodes, without it ever having been suspected, and their ill health over a period of time laid to other causes. I have had in my own practice two girls from whom normal appendices were removed several years ago, but the omentum and mesenteries were full of tuberculous nodes from the size of a buckshot to that of a marble. Both of these girls were in good health, and no one would have suspected that they were infected with tuberculosis. After their operations they had no particular treatment other than ordinary right living, and they have apparently overcome the

infection as they are both perfectly well, and leading the usual active lives of girls of eighteen. If their abdomens had not been opened, it is probable that no diagnosis of tuberculosis would ever have been made. There must be many such children, and the prognosis is in general good, provided the infection is not too extensive.

TUBERCULOSIS OF THE KIDNEY

THIS girl is nine years of age. Her past history is irrelevant.

On April 15, 1928 she passed bloody urine twice. Her mother, a very intelligent woman, was sure it was blood, and there was enough of it to color the water in the toilet a deep red. This was not accompanied by pain, or symptoms of any sort, nor was there any fever. I saw her the next day. Physical examination was entirely negative except that the right kidney was palpable This was apparently not large, and was not tender. The urine was slightly cloudy, and contained a very slight trace of albumin, and a good many pus-cells, some in clumps, with a very rare red blood-cell. In the absence of pain as any other sign or symptom of stone, the diagnosis of pyelitis was made, and she was started on large doses of potassium citrate, with forced fluids. This was continued for about ten days with practically no improvement in the urinary condition, so she was then given 30 grains of hexamethylenamin a day with acid soda phosphate. This was later increased to 45 grains a day, and was continued for nearly a month with very little result.

The urine remained consistently somewhat cloudy, and there was always a small macroscopic sediment of pus. About June 20th she went away for the summer, and was then started on caprokol, 1 teaspoonful four times a day. Under this treatment the condition of the urine improved somewhat, but it still contained a moderate amount of pus. The child herself was perfectly well, led a normal life, and gained 4 pounds during the summer. She returned from her vacation about the middle of September, in excellent general condition, but with the urine still the same. This was never very cloudy, and sometimes would be almost clear, but always showed considerable numbers of pus-cells under the microscope.

In view of the fact that she had a long-standing pyuria, even if it was only of slight degree, which had not been appreciably influenced by intensive treatment, it was decided to do a cystoscopy and pyelography to ascertain whether or not there might be some anatomic anomaly of the genito-urinary tract which might account for the obstinate character of the pyuria. She was sent to the private ward of the Children's Hospital for complete investigation.

Cystoscopy was done by Dr. W. E. Ladd. The bladder and ureteral orifices were normal. The ureters were catheterized, and slightly cloudy urine came from both. Roentgenograms after injection of the pelves of the kidneys showed nothing abnormal. Urine from both of the kidneys was sent to the laboratory for guinea-pig inoculation, although tuberculosis was not suspected, and the pelves of the kidneys were washed out with hexylresorcinol solution.

The phthalein test was 60 per cent., and the blood non-protein nitrogen 33 mg., both within normal limits. The tuberculin test was positive. In short, nothing of importance was found, and the patient was discharged.

We were somewhat surprised when we received the report of the guinea-pig inoculation some weeks later. The pig into which the urine from the right kidney had been injected was riddled with tubercles, and the tubercle bacillus was isolated. The other pig showed no lesions. It was rather hard for us to believe that a child in such perfect health, and who had gained 4 pounds in weight during the summer, could have tuberculosis of the kidney, but the guinea-pig test is most reliable, and we were sure there had been no mix up of specimens.

Most authorities are agreed that the best treatment of unilateral tuberculosis of the kidney is removal of the kidney, that tuberculosis in this location practically never heals, and that the earlier the nephrectomy is done, the better for the patient, for with delay there is great danger of infection of the other kidney. So we were confronted with the somewhat disturbing situation of removing a kidney from an apparently well child. She was seen in consultation by Dr. A. H. Crosbie, a urologist, who strongly advised immediate removal of the right kidney, but suggested another ureteral catheterization before doing this, in order to be absolutely sure that no pus was coming from the other kidney, in spite of the negative guinea-pig inoculation. At the second ureteral catheterization the urine from both kidneys was almost clear macroscopically (a dilute urine), but microscopically that from the right kidney showed a good many pus-cells, while that from the left showed numbers of large epithelial cells, but no pus. These probably came from irritation of the ureter by the catheter.

On November 21st, seven months after the onset of the trouble, the right kidney was removed by Dr. W. E. Ladd. Upon delivery it did not appear enlarged, and looked and felt normal. On section it showed a good many pinhead-sized tubercles in the mucous membrane of the upper portion of the pelvis.

Discussion.—One sees so much pyelitis in female children that the possibility of a pyuria being tuberculous in origin is not ordinarily thought of, which is the chief reason for presenting this case. Hematuria at the onset, as it occurred here, is not usual in a common pyelitis, but there did not seem to be enough evidence at that time to justify ureteral catheterization. The long-continued pyuria, however, in spite of adequate treat-

ment, is an indication for pyelography and ureteral catheterization, and it should be done on every long-standing, obstinate case of pyelitis, as has been so well pointed out by R. M. Smith, C. G. Mixter, and others. What one is likely to find is not tuberculosis, but various anomalies of the genito-urinary tract. This case emphasizes the fact, however, that tuberculosis should always be borne in mind. The immediate prognosis for this girl is excellent, and if she does not develop tuberculosis in her remaining kidney, or elsewhere in the body, she will probably do very well.

JAUNDICE OF LONG DURATION IN A NINE-YEAR-OLD GIRL

THIS girl's symptoms have covered a period of five years. There is nothing of importance in her past history, previous to the condition from which she is now suffering, nor in her family history.

In August, 1923 slight jaundice was noted. This came on gradually, without vomiting or other symptoms of illness. In October, 1923 her tonsils and adenoids were removed, followed by a good deal of bleeding. She was examined in December, 1923, by her family physician, who found that her liver was somewhat enlarged. Her urine was dark at times, at others apparently normal. The mother does not remember whether or not the stools were clay colored. The jaundice, in January, 1924, had cleared somewhat, but had not gone entirely. In February, 1924, about five months after the onset of her jaundice, an enlarged spleen was first noted. She had had occasional nosebleeds, and in October, 1924 blood was first noticed in her urine. This occurred every few weeks for a period of two or three days, but never persisted. She felt fairly well, ate well, and was able to go to school. She entered the wards of the Children's Hospital in January, 1925, for observation.

She was moderately jaundiced, there were two small "spider" telangiectases on the face, a few purpuric spots on the face and hands, and several large "black and blue" spots on the lower legs. Her liver was considerably enlarged, being easily palpable 3 inches below the costal margin, rather hard and non-tender. The spleen was felt about 2 inches below the costal margin. There was nothing else noteworthy about the physical examination. She has had no ascites at any time.

Laboratory work was as follows:

Urine.—Bright red—albumin, slight trace—no sugar—no bile or urobilin. The sediment showed large numbers of red blood-cells.

Blood.—Hemoglobin 65 per cent.; red blood-cells, 3,616,000; white blood-cells, 5000. A normal differential count and an essentially normal red cell picture. Wassermann test and blood-culture negative.

Fragility Test.—Hemolysis began at 0.55 per cent. and was complete at 0.37 (normal).

At no time while she was in the hospital did she have any fever.

She has been followed in the Out-patient Department since her discharge from the wards and has been in reasonably good general health, well enough to go to school.

She was last seen June 28, 1928. At that time the scleræ were very slightly yellow, but the skin was jot jaundiced. The spleen was palpable, hard and smooth, about 2 inches below the costal margin. The liver, instead of being enlarged, as it had been in the beginning, was small. It was not palpable, and the upper border of dulness was at the sixth rib. The urine showed a very slight trace of bile.

Discussion.—We have here a girl who has been slightly jaundiced over a period of five years, with an enlarged liver in the beginning, and an enlarged spleen at present.

Such a clinical picture can be explained only by three diagnoses: Syphilis, chronic familial hemolytic icterus, or Hanot's cirrhosis of the liver. Syphilis is ruled out by the negative Wassermann test, and hemolytic icterus by the normal fragility of the red blood-cells, the fact that the urine contains bile, and that the stools have sometimes been clay colored. This means obstructive instead of hemolytic icterus. Although Hanot's cirrhosis is excessively rare in children it may occur, and the train of symptoms this child has had and the physical findings she has shown seem to fit in with this diagnosis better than with any other. There is no effective treatment, and the ultimate prognosis is not good, although she may continue about as she is now for several years more.

CLINIC OF DR. SAMUEL A. LEVINE

PETER BENT BRIGHAM HOSPITAL

A CASE OF ULCER OF THE ESOPHAGUS WITH EXTRAORDINARY MEDICAL EXPERIENCES

AN account of the following case is discussed in considerable detail because of the numerous points of interest that it manifests. There are several lessons to be drawn from the entire experience which certainly have proved very instructive to the various physicians who were involved at one time or another during this patient's illness. It has proved particularly instructive to me, probably because I had the largest share of the burden during the time that the diagnosis was obscure. As we shall see a little later a great many physicians and surgeons, including myself, were at a loss to explain the patient's symptoms. All of us were wrong, one thinking that it was angina pectoris, another that it was gall-stones, a third that it was neurosis, a fourth that it was cancer, etc. It is very impressing that during all the wanderings of the patient from one competent physician to another he never lost faith in the medical profession and even after it became clear that they were all wrong, the patient still felt satisfied that each man had done his best in trying to get at the bottom of his troubles. At one time he was even sent to an osteopath at my suggestion with the hope of obtaining relief from the pain and distress that he suffered. This proved of no avail. At another time the condition was diagnosed as cancer, even after microscopic examination of the section of tissue that was removed. With this sword of Damocles hanging over his head the patient courageously continued to follow medical advice, retained his faith in the medical profession and was rewarded for his efforts when it finally became clear that he had a benign curable condition.

The patient was a business man, aged forty-eight, who was first seen September 7, 1920. At this time his chief complaint was a terrible pain in the chest, somewhat more to the right of the midline than to the left. He stated that this began eight months previously and would follow a feeling of heart-burn. The pain would localize itself particularly in the sternum and spread laterally, and occasionally to the head. At first it was rather mild, but during the previous few weeks it had grown severe and was almost continuous. Sodium bicarbonate used to help him a good deal, but latterly it had only given him temporary relief. The pain would frequently wake him from sleep. It would never radiate to his arms, but occasionally to the left shoulder. He never vomited until the day before he was first seen. It was not aggravated by exertion. It used to last fifteen minutes, but now it continued for hours. There was no abdominal pain and no other important symptoms. There had been no dyspnea on exertion or swelling of the feet. He had rheumatic pains in his limbs off and on. Nocturia once for several years. The past history was negative for infections except for frequent tonsillitis. Tonsillectomy was performed one year before. The family history was entirely negative.

Physical examination showed a well-developed individual. Pupils were normal. No glandular enlargement. Heart was not enlarged. Action was regular. There was a slight systolic murmur at the apex and at the pulmonary area, where a definite pulsation could be seen. The heart-sounds were of good quality. No increase in submanubrial dulness. Blood-pressure was 112 mm. systolic and 70 mm. diastolic. Lungs were negative except for a moderate number of crackling râles at the right base. Abdomen showed no masses or tenderness. Liver and spleen could not be felt. No peripheral edema. Deep reflexes were normal. Electrocardiograms were normal except for left ventricular preponderance. Urine showed no albumin or sugar. The specific gravity was 1.022 and the sediment was normal.

The patient at this time came to see me because his physician was concerned about the possibility of angina pectoris. I felt quite certain that he did not have angina pectoris. The minor heart findings were the only positive ones on examination and I felt that he had a slight chronic myocarditis, but not sufficient to explain the symptoms. He had previously had *x*-ray examinations which were essentially negative although the roentgenologist brought up the possibility of adhesions around the gall-bladder, or a duodenal ulcer.

A period of rest in bed did not alter the symptoms and at no time did he get any prompt relief from taking nitroglycerin. The symptoms continued, despite various dietary courses that he followed. He therefore went to New York City to interveiw physicians there, but without any success. A few months later he went to a hospital in Baltimore where he remained six weeks. During the first four weeks of his stay he had daily drainage of the gall-bladder by the Meltzer-Lyon method, as a result of which he grew desperately sick and it required two weeks after this treatment for him to recover sufficiently to leave the hospital. While there the prevailing diagnosis was some form of gall-bladder disease, probably chronic cholecystitis. He was observed during his stay by most competent men, both medical and

surgical, and it was felt that if the symptoms continued much longer an operation on the gall-bladder would be indicated.

On his return to Boston I found that his symptoms were essentially unchanged. In June, 1922 he was having daily pains in his chest which would radiate to the back of the neck, to the left axilla, and to the left shoulder. He noted that the pain would frequently come while sitting in the barber chair. He made the casual observation, which was not sufficiently appreciated at this time, that he occasionally had a choking sensation on eating bread. He also observed that during long periods of time while playing cards, which he thoroughly enjoyed, he would never have pain. Then in the still of the night he might have to pace the floor because of the distress in his chest. Physical examination had not changed, and believing that the entire illness was functional in origin, I sent him to a competent neuropsychiatrist who had had unusual success with difficult neurotics. Under his care no improvement whatever resulted.

In December, 1922 I thought it wise to have him enter the Peter Bent Brigham Hospital for more careful examination. Because the problem seemed to be an obscure one and refractory to treatment, the possibilities of rare conditions like cervical cord tumor or syphilis of the central nervous system with a negative blood Wassermann had to be ruled out. During his hospital stay he was thoroughly studied. *x*-Ray examination of the entire gastro-intestinal tract was negative. The spine showed no abnormal changes. Lumbar puncture was performed which showed a negative Wassermann and globulin test, and no increase in the cells. The dynamics of the spinal fluid were normal. There was a normal response to pressure over the jugular veins. Stool examinations showed no occult blood. Counts of the red and white cells were normal. The stained smear was also normal. Repeated Wassermann tests were negative. Phthalein test showed 72 per cent. excretion in two hours. The heart findings were the same as on the first examination. The abdomen showed slight tenderness in the epigastrium. A surgeon who saw him in consultation at this time summarized the situation as follows: "An introspective somewhat neurasthenic person with possibly some chronic gall-bladder trouble, certainly insufficient to demand operative treatment." Gastric analysis showed a normal fasting content and no evidence of obstruction and a test-meal showed normal acidity. Bile drainage showed nothing unusual. Bacteriologic examination of the various portions of bile showed no growth of any organisms. On discharge from the hospital the patient was told to take six small meals a day to be followed in one hour by a powder containing 2 gm. of sodium bicarbonate and 0.6 gm. of magnesium oxid.

Believing that the condition was mainly functional, he was told to keep away from all doctors, as none of us had been of any help to him during the past year. He tried this for two months, but his symptoms continued. He persisted in returning to me, although I had told him a great many times that I could find nothing wrong with him and that I had no particular suggestions for therapy. Possibly this very frankness made him continue to seek my advice.

In April, 1923 I advised him to see a physician who was particularly studying dysfunctions of the liver. He found no evidence of pancreatic

insufficiency, although he thought there was some hepatic insufficiency. During his examinations he did detect transitory spasms in various parts of the pyloric end of the stomach, the first portion of the duodenum, and in the esophagus. His summary was as follows: "It seems to me that the entire history and clinical picture fits in with that of a neurosis based on the brother's death. If treatment had been carried out before the development of the esophageal spasm had occurred, a cure would have been more easily effected. The present symptoms are the result of esophageal spasm. The fact that alkaline powders relieved them and that they occur on an empty stomach is not against this diagnosis. That the patient can swallow during the spasm is also not against the diagnosis; for during pain and esophageal spasm observed under the fluoroscope the patient could swallow. Alkaline powders and the act of swallowing often relieve spasm. Treatment: Atropin, esophageal sounds, hourly feedings with frequent dosage with alkaline powders, and hydrostatic bag dilatations."

This was the first intimation that there might be something wrong with the esophagus. The reason that it was discovered at this time was because fluoroscopy of the esophagus happened to be carried out during the time when the patient was in pain and showed spasm. Numberless previous examinations of the esophagus had always failed to show any abnormality because they were done at a time when the patient was not having active pain. The lesson that was learned from this experience was that *x*-ray examinations were useless when carried out in the routine fashion, but that when the presenting symptom of pain was reproduced by having the patient swallow coarse food, then the underlying origin of the trouble was uncovered.

From this point on it became a problem of discovering the cause of the esophageal spasm. It seemed proper to have the esophagus examined directly and when this was suggested to the patient he became quite anxious to have it done. This matter was discussed with a most competent specialist and after reviewing all the data he felt that it was so unlikely to discover anything of importance that he advised strongly against esophagoscopy. He felt that the patient, who was a fairly well-to-do business man, had already seen too many doctors and that the fact that he could afford to pay for medical attention was no reason for putting him through unnecessary examinations. I mention this to describe the general attitude of a most competent and intelligent throat specialist and to reflect the unlikelihood at that time of finding anything abnormal in the esophagus. Because the patient was insistent in leaving no stone unturned in the attempt to get at the bottom of his trouble, direct esophagoscopy was carried out.

One can readily picture the surprise that we experienced when a tumor mass the size of a peach-stone that looked like a cancerous growth was found in the posterior wall of the esophagus, at the level of the middle of the heart. It was my duty to meet the family immediately after this operation and to tell them the sad news. It seemed particularly difficult because I had repeatedly told them that I thought that there was nothing organically wrong with the patient. A specimen of this mass was removed and the pathologic report indicated that it probably was malignant. This report and the general cancerous appearance made the diagnosis of cancer of the esophagus seem

so likely that the surgeon frankly told the patient what he had. He was advised to prepare his affairs for a fatal outcome. A few days after he left the hospital the patient visited me at my office for further advice. Seeking for some method of raising his spirits and maintaining a ray of hope in the face of an apparently malignant and fatal disease, I made the fortunate remark to the patient that no physician or surgeon who had any extensive practice was always infallible and that the best of us occasionally were wrong. I added that he might just as well get to work on the idea that in this case medical judgment had so far erred.

At about this time a publication had recently appeared on the surgical treatment of cancer of the esophagus in which it seemed that as a result of a two-stage drastic operation one patient out of eighteen had had a most favorable recovery. Our ill-fated patient was therefore sent to New York for further advice. Here as a result of direct examination of the esophagus and pathologic examination of a small section that was removed, the diagnosis of a benign ulcer of the esophagus, possibly precancerous, was made. Dr. Mandlebaum, after studying the pathologic sections, came to the following conclusion: "The larger piece of tissue contains numerous glandular structures resembling those normally found in the mucous membrane of the stomach. Aberrant glands of this type are frequently found in the lower portion of the esophagus. A few areas of chronic inflammatory tissue are seen. The smaller fragments are covered by high cylindrical epithelium, not usually present in the esophagus. The surface of the specimen is thrown into numerous folds resembling the appearance seen in benign papillomata in other portions of the body, but there is no indication of the presence of a true tumor. Nothing of a malignant character is present in any of the specimens submitted for examination." At this point the microscopic slides were sent to Professor Frank B. Mallory for his opinion. He also felt quite certain that it was not a malignant tumor. The three possibilities that he suggested were: (1) Islands of gastric mucosa; (2) adenomatous and cystic structures in the region of the diaphragm connected with the embryonic development of the lungs from the esophagus; (3) some abnormality of the common mucous glands of the esophagus.

This investigation put quite a different turn to the entire problem. While still in New York the surgeons there advised an operation because they felt that it was a favorable case for an absolute cure. They emphasized the feature that the lesion might be precancerous. Shortly before the date set for the operation I was asked to review the entire problem with the patient and the surgeons, and came to the conclusion that inasmuch as the condition was most likely an aberrant gastric ulcer with redundant growth, situated in the esophagus, it was not unlikely that a carefully regulated course of treatment for gastric ulcer following the Sippy régime might be worth a trial. It certainly seemed wise to avoid an operation which carried with it such a terrifically high mortality. He therefore was advised to return to Boston and to again enter the Peter Bent Brigham Hospital. Here he remained for four weeks and was given a strict course of ulcer treatment, at first using milk and cream mixtures hourly with the customary frequent alkaline powders. Curiously enough all symptoms disappeared during this month. The patient

felt perfectly well and had no pain whatever. This was the first time in months that he remained free from pain for any appreciable interval and it seemed as if we were to accomplish a cure. Shortly after leaving the hospital, however, all the symptoms returned.

During his previous wanderings the patient had been to Battle Creek, Michigan, and there had learned that one might have syphilis and not know it and even show a negative Wassermann. He therefore insisted that he be given a course of antiluetic treatment. He received six weekly intravenous injections of neosalvarsan and took protiodid of mercury, by mouth, with no improvement in his condition.

In June, 1923 while the patient's symptoms were somewhat ameliorated, by taking frequent alkaline powders, he was sent to Dr. Chevalier Jackson of Philadelphia. Here the diagnosis of superficial ulcer of the esophagus was confirmed and it was considered non-malignant. During the following five years he had fifty-two examinations and treatments performed, at first returning every week or two, later every month or so, and finally at less frequent intervals. Generally the lesion was treated locally by the application of argyrol or 20 per cent. silver nitrate. During one of these examinations a piece of litmus paper applied to the ulcerated area showed a marked acid reaction. The ulcer was slow in healing, but gradually granulation tissue grew in from the edges, and finally, in July, 1928, no ulceration could be seen. At the site of the old ulcer was a white scar. At present the patient is practically well, doing his work daily, and, in fact, has not been confined to bed at any time during the past five years.

Summary.—The salient features in this case may be summarized as follows: A middle-aged man complained of pain in the sternum with slight radiation to the left. There was some reason to consider the possibility of angina pectoris, but the pain was not related to effort. In many respects it resembled chronic gall-bladder disease. It finally turned out to be due to redundant and ulcerated gastric mucosa in the posterior esophageal wall. During many months before the correct diagnosis was established the patient was examined by numberless internists, surgeons, and roentgenologists. I had come to the conclusion that the condition was entirely a neurosis and had repeatedly urged the patient to keep away from physicians none of whom up to this time had helped him. His persistence and confidence in the medical profession were the outstanding features in this whole experience. The first clue to the proper diagnosis was obtained only when the patient was fluoroscoped at a moment when he was in pain. This is one of the most instructive lessons to be

drawn from this case. Another point that deserves emphasis is the general attitude of hopefulness that was maintained even after the diagnosis of cancer was made, from both the gross and microscopic examination of the mass. The occasional fallibility of even expert medical judgment is well illustrated in the above case, for the patient recovered completely.

CLINIC OF DRS. HERRMAN L. BLUMGART AND HAROLD E. MACMAHON

FROM THE MEDICAL SERVICE OF THE BETH ISRAEL HOSPITAL AND THE DEPARTMENT OF PATHOLOGY OF THE BOSTON CITY HOSPITAL

BRONCHIOLITIS FIBROSA OBLITERANS: A CLINICAL AND PATHOLOGIC STUDY

THE patients to be presented today illustrate one of the most perplexing problems in the diagnosis of lung conditions. In order properly to interpret the patient's clinical manifestations, we shall review briefly the clinical and pathologic findings observed in this condition in recent years and include 5 cases of our own.

Definition.—Bronchiolitis fibrosa obliterans is a disease which, as the name implies, is characterized by connective-tissue proliferation in the bronchioles in response to local injury.

History.—The disease was recognized first by Lange,[1] in 1901, as a distinct pathologic entity differing from similar conditions such as indurating pneumonia, disseminated bronchopneumonia, and organizing pneumonia. He described the pathologic findings in 2 cases. Fraenkel, in 1902,[2] reported a similar case, describing more fully the clinical aspects. Since then occasional isolated cases have been published, but the total number observed is still exceedingly small.

Etiology.—The etiology is extremely variable. Cases have reported following measles,[8] whooping-cough,[3] inhalation of the fumes of hydrochloric acid or nitric acid,[2, 6] and the inhalation of foreign bodies.[5] According to Friedrich Müller,[7] the disease may occur in the absence of any specific etiologic factor following an acute or subacute bronchiolitis. The etiologic factors have but one characteristic in common—a predominant injury to the

walls of the bronchioles. The condition may occur at any age, and both sexes are equally susceptible.

Morbid Anatomy.—Gross Pathology.—In gross, the lungs so closely simulate miliary tuberculosis or minute disseminated foci of tuberculous pneumonia that, as was done in the first case reported by Lange,[1] extensive and detailed search usually is made by the pathologist to discover the original focus of the "tubercular" lesion. The nodules of bronchiolitis fibrosa obliterans are grayish white, miliary in size, firm to the touch, and, in their most characteristic distribution, are scattered uniformly throughout both lungs. By means of the hand lens the lesions may be differentiated from those of miliary tuberculosis by the fact that they are somewhat irregular in outline instead of round, and also, on close inspection, fine white streaks may be seen to radiate in all directions from the centers of many of the larger nodules. These streaks represent newly formed connective tissue extending in a stellate manner into the adjacent parenchyma. Careful inspection may also reveal a tiny pore in the center of the nodule which represents all that remains of the lumen of the bronchiole.

Microscopic Pathology.—With the aid of the microscope the unusual character of the pathology of bronchiolitis fibrosa obliterans becomes clear. The characteristic lesion is the nodule which consists of an injured bronchiole whose lumen is partially or completely obliterated by organizing granulation tissue, and whose wall is surrounded by an irregular growth of newly formed fibrous tissue. In this reparative process of the wall of the bronchiole strands of connective tissue actually penetrate both the muscularis and the elastic tissue fibers and are continuous with the fibroblasts of the peribronchial tissues. The growth of connective tissue into the lumen assumes various forms. In some instances it forms crescents only partially obliterating the lumina of the bronchioles; in others, it grows in from the wall on all sides so that one is in reality dealing with narrowed bronchioles, and finally the connective tissue may completely obliterate the lumina. *This pathologic process, which involves essentially the bronchiole, its lumen, and the surrounding bronchiolar*

tissue, differentiates bronchiolitis fibrosa obliterans from the other types of pulmonary pathology.

The sequence of histologic changes in the fibrosing bronchiolitic process has been carefully studied. First there is a simple catarrhal inflammation involving the surface epithelium as occurs so commonly in a mild bronchiolitis. Later, the epithelium may undergo necrosis with widespread desquamation. In this stage the reaction extends more deeply, involving the membrana basalis, the elastic and muscle fibers, and the adjoining connective tissue. The tissues are edematous and are heavily infiltrated with an acute inflammatory exudate containing an unusual amount of fibrin. This acute reaction may progress until small foci of necrosis appear within the wall. These may fuse until finally, though rarely, the entire bronchiole is represented by a ragged wall of necrotic tissue leading, in some cases, to actual bronchiectasis and cavitation.

The process of repair usually begins before such extreme necrosis has developed and the epithelium regenerates, partially covering the denuded surface of the lumen. But here and there, where injury of the wall has been more extensive, dense fibrin gathers in the tissue spaces and, also, within the lumen. Since liquefaction of this fibrin takes place slowly, the adjacent fibroblasts are stimulated to proliferate into the fibrin so that, with the aid of newly formed capillaries, complete organization of the lesion finally results. In a few instances a still later stage may be observed in which the granulation tissue closely resembles adult connective tissue and the narrowed, distorted lumen of the bronchiole becomes completely lined by normal ciliated columnar epithelium. It is this latter possibility which may explain some of the cases which recover.

The ultimate consequences of the connective-tissue plugs in the bronchioles depend upon whether the obliteration is partial or complete. If the obliteration is complete, the distal alveoli become atelectatic and sometimes become organized. This secondary organization of the collapsed alveoli can occur only in the more protracted cases when life is prolonged by virtue of a relatively normal portion of pulmonary tissue.

If the bronchioles are but partially obliterated, a different train of events takes place. Since inspiration is an active process and expiration a passive process, the partially obliterated bronchioles assume a valve-like action so that the alveoli tend to become distended with air. This in time leads to true alveolar emphysema.

Clinical Manifestations.—Symptoms.—The symptoms are greatly influenced according to whether the disease is caused by the inhalation of gases, by influenza, or by other acute infectious diseases. In its simplest form as following the inhalation of gases or when, as in Case I of this series, it is due to an acute infectious agent, the onset of the condition is signalled by chills or chilliness, slight or moderate fever, extreme dyspnea, and cyanosis, and a dry, hacking cough with little or no sputum. The temperature may fluctuate considerably and may be subnormal part of each day. After several days the cough may subside, the dyspnea and cyanosis lessen, and the temperature may return to normal. These changes coincide with the subsidence of the catarrhal inflammation as seen pathologically. Rarely the patient may recover, though usually one observes a recrudescence of the symptoms and signs after two or three weeks. The dyspnea and cyanosis increase, occasional medium moist râles may be heard everywhere over both lungs, the temperature becomes more elevated and finally the patient dies of asphyxia. This period of increasing cyanosis and dyspnea corresponds to the connective proliferation obliterating the lumina of the bronchioles.

Physical examination usually shows no areas of definite dulness or of bronchial breathing except as a terminal manifestation. Many moist râles may be heard everywhere over both chests, and expiration is relatively prolonged.

Both miliary tuberculosis and bronchiolitis fibrosa obliterans show dyspnea, cyanosis, and absence of definite areas of dulness or bronchial breathing. Both may show occasional crepitant râles. The differential diagnosis can be settled in doubtful cases only by repeated examinations of the sputum, careful consideration of the former history of the patient and examination of the

eye-grounds. It is important in any case in which the question of miliary tuberculosis arises to consider the possibility of bronchiolitis fibrosa obliterans for it is not improbable that certain rare instances of recovery from miliary tuberculosis may, in reality, have been cases of bronchiolitis fibrosa obliterans.

When the lesions are limited to a portion of the lungs, the differential diagnosis may be decided by the fact that with actual spread of the lesion according to *x*-ray the patient, if he has miliary tuberculosis, should become progressively worse; whereas, in reality, with organization of fibrin in adjacent alveoli and the arrest of the infectious process he steadily improves.

The following cases illustrate various types of the disease, but have one characteristic in common, *i. e.*, a predominant lesion of the bronchiolar wall.

Case I.— *History.*—The patient, E. L., was a girl of eighteen who entered the hospital on October 23, 1927 complaining of fever, cough, and general malaise, two weeks in duration. She had had chickenpox at the age of two, measles at five, whooping-cough at eight, and mumps at fourteen. After each of these illnesses she had regained full health. Seventeen days before entering the hospital she first noticed the onset of a "cold." She continued to attend school, but was finally forced to take to bed fourteen days previous to entry. Since that time her cough gradually had become worse. She had raised a considerable amount of thick, greenish-yellow sputum which had never contained blood. She had felt flushed and hot, and occasionally had experienced pain over the front part of the right chest on coughing. On two occasions she had vomited.

Physical examination showed a well-developed and nourished girl, propped up in bed, breathing with great difficulty. Her face was cyanotic and the alæ nasi dilated with inspiration. The skin showed grayish cyanosis. The throat was injected. Purulent sputum was adherent to the posterior pharyngeal wall. Expansion of the chest was equally diminished on both sides. On examination of the lungs no dulness or other signs of consolidation could be made out. Medium, crepitant râles were heard over the entire chest, anteriorly and posteriorly. The finger-nails showed cyanosis, but there was no clubbing of the fingers.

x-Ray examination showed a diffuse inflammatory process consistent with either miliary tuberculosis or a very diffuse bronchopneumonia.

The sputum was repeatedly negative for tubercle bacilli.

Examination of the blood showed the red cells 4,390,000 per cubic millimeter; the white cell count 8250 to 11,000 per cubic millimeter; the hemoglobin 75 per cent. The differential count was 64 polymorphonuclear cells; 30 lymphocytes; 4 large mononuclear and 2 eosinophilic cells per hundred. The stained smear revealed no abnormalities. The urine contained 0.2 per

cent. sugar, a trace of albumin, many pus-cells, no casts. Two blood-cultures were negative. On repeated examination of the blood there was no leukocytosis. The temperature curve during the eight days in hospital was markedly irregular, varying between 100° and 104.8° F. The pulse-rate varied from 120 to 160 per minute; the respiratory rate, 40 to 60 per minute.

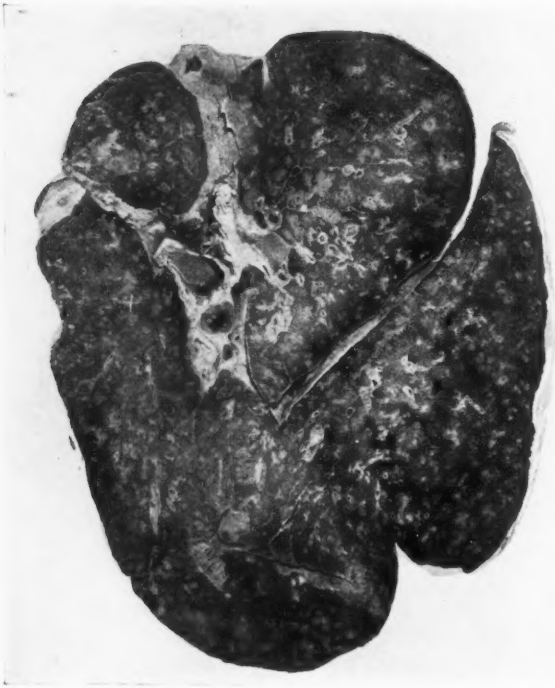

Fig. 20.—Section of the lung from Case I showing the size, shape, and disseminated distribution of the lesions. Alveolar emphysema is present in intervening parenchyma.

In spite of the administration of oxygen the patient became more dyspneic, cyanotic, prostrated, and died October 30, 1927, on the twenty-second day of her illness.

The clinical diagnosis was miliary tuberculosis of the lungs.

Autopsy Report.—*Gross Pathology.*—Both lungs were moderately distended with air and were gray, soft, and crepitant. The lower lobe of the right lung was coated with a delicate fibrinous exudate. Minute nodules,

firm, granular, and yellowish gray, measuring 1 to 2 mm. in diameter and resembling miliary tubercles, were scattered thickly and uniformly throughout both lungs (Fig. 20). Careful examination of some of these tubercle-like structures revealed a central pore, pinhead in size. The shape of some of the nodules was round and regular, while others had an irregular periphery with gray lines radiating into the adjacent lung parenchyma. The bronchi and larger bronchioles were engorged and filled with frothy, thick, blood-tinged fluid.

The gross pathologic diagnosis was miliary tuberculosis of the lungs.

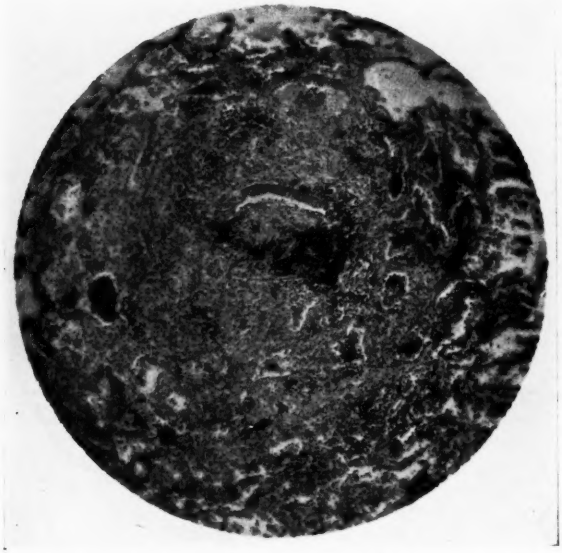

Fig. 21.—Low-power photomicrograph showing bronchiole with its lumen almost completely obliterated by a fibrous plug. There is a chronic inflammatory reaction in peribronchiolar tissue. (× 100.)

Microscopic Pathology.—In none of the sections were we able to find a trace of tuberculosis. Instead, the scattered focal lesions throughout the lungs were simply sections of small bronchioles showing a chronic inflammatory reaction. The lumina of the bronchioles were partially or completely obliterated by organizing granulation tissue. In a few areas a dense fibrinous exudate filling the alveolar spaces bordering the bronchioles showed beginning organization (Figs. 21, 22). The remaining lung tissue, except for a little coagulated albumin in some alveoli and moderate alveolar emphysema, was negative. The larger bronchioles showed slight catarrhal inflammation and

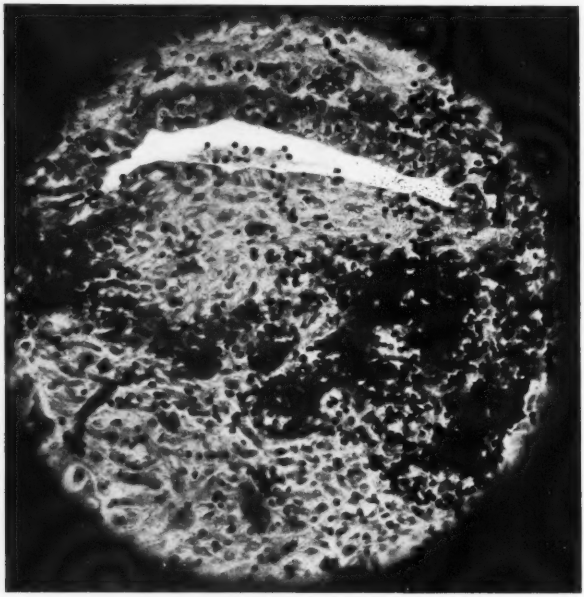

Fig. 22.—A higher power photomicrograph of bronchiole in Fig. 21. Lumen reduced to a mere slit. Epithelium beginning to grow in at periphery over surface of connective-tissue plug. Extravasated red blood-cells within newly formed connective tissue. (× 300.)

contained an acute inflammatory exudate. Few small clusters of alveoli were distended with a well-preserved acute inflammatory exudate.

Microscopic Diagnosis.—*Bronchiolitis fibrosa obliterans.*

Discussion.—The presence of irregular fever, cough, dyspnea, and grayish cyanosis, accompanied by marked prostration, suggested the possibility of pulmonary miliary tuberculosis. This possibility was further emphasized by the absence of signs of consolidation, the presence of medium moist râles, and the normal white blood-cell count without predominance of polymorphonuclear neutrophils. The *x*-ray examination of the chest showed a process consistent with miliary tuberculosis of the lungs. In spite of repeated examinations of the sputum, no tubercle bacilli could be found. The persistent absence of acid-

fast organisms in this case represented the only basis for diagnostic differentiation of the two conditions.

The findings in this patient are characteristic of bronchiolitis fibrosa obliterans in its purest form.[1, 2, 7] The pathologic process is limited almost entirely to the bronchioles of both lungs, the parenchyma being essentially uninvolved. The infection caused actual necrosis of the lining epithelium and subjacent tissues, thereby stimulating connective-tissue organization. This connective tissue, which gradually obliterated the air-passages, caused the increasing cyanosis and dyspnea. Had the process continued and completely obliterated the bronchioles, the distal alveoli would have collapsed and, in the presence of infection, undergone an inflammatory reaction with organization. In this patient, because the bronchioles were so generally involved, death ensued before the distal alveoli had shown an appreciable change.

Etiology.—Since the only bacteriology done on this case during life was the careful search for tubercle bacilli, and the routine typing of sputum which was reported as Pneumococcus Type IV, we are unable to state the nature of the infecting agent.

Case II.—*History.*—The patient, W. S., was admitted, December 12, 1925, on the contagious service, where a diagnosis of mild scarlet fever was made. He had always been well. The course of the scarlet fever was typical, but he contracted varicella, and the temperature did not return to normal until the seventeenth day. On the fifty-fourth day after admission paroxysms of coughing were noted and a tentative diagnosis of pertussis was made. The paroxysms of coughing continued with normal temperature, pulse, and respiratory rate until the sixty-fourth day of the patient's stay in the hospital, when the temperature and pulse became elevated. Four days later the respiratory rate increased above normal, the patient raised purulent sputum, and the lungs showed numerous fine, medium, and coarse râles. *x*-Ray examination showed small, scattered areas of density. Although there were periods of temporary improvement, these symptoms and signs increased in severity during the next three weeks, and the patient died on the seventy-eighth day of his stay in the hospital. All blood-cultures were negative.

The clinical diagnosis was whooping-cough, bronchopneumonia.

Autopsy Report.—*Gross Pathology.*—Gross inspection of the lung indicated a rather diffuse congestion of both lower lobes, with some consolidation of the right upper lobe, and a fairly normal upper left lung. There were minute yellow nodules on the cut surfaces of the lower lobes suggesting miliary tubercles.

Microscopic Pathology.—Many sections taken from different portions of the lungs showed an inflammatory reaction of long standing, centering about the bronchioles and extending out into the adjacent alveolar spaces. In some places the reaction was quite acute; in others, the picture was of a later stage of inflammation with many phagocytic endothelial leukocytes in the alveolar spaces. The reaction in the bronchioles varied; in some the epithelium had desquamated with little or no reaction in the underlying tissue;

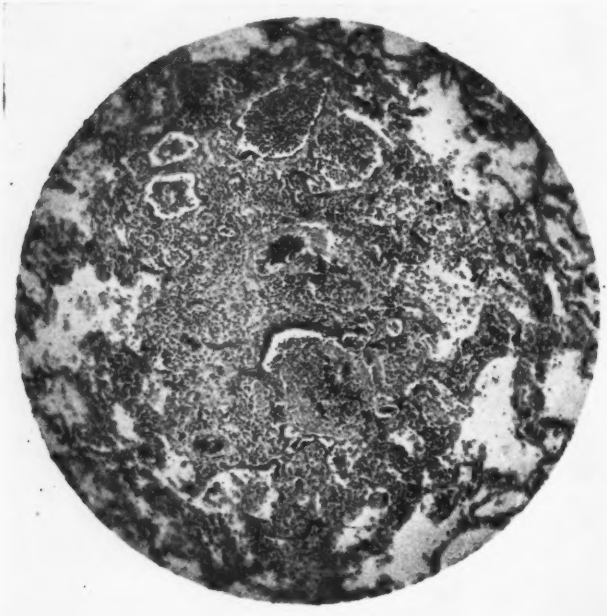

Fig. 23.—Low-power photomicrograph showing small bronchiole nearly occluded by a plug of a granulation tissue. Chronic inflammatory reaction in adjacent tissue. Some of more distant alveoli contain an acute inflammatory exudate. (× 100.)

whereas in others the walls showed necrosis and hemorrhage followed by a diffuse proliferation of connective tissue extending into and obliterating the lumina of the bronchioles. This fibrosis involved the wall and the surrounding peribronchiolar tissue and at times was seen within the walls and alveolar spaces of adjacent atelectatic alveoli. Such a diffuse reaction, involving so much of the stroma, simulates a focus of organizing pneumonia (Figs. 23, 24).

Microscopic Diagnosis.—*Bronchiolitis fibrosa obliterans. Bronchopneumonia.*

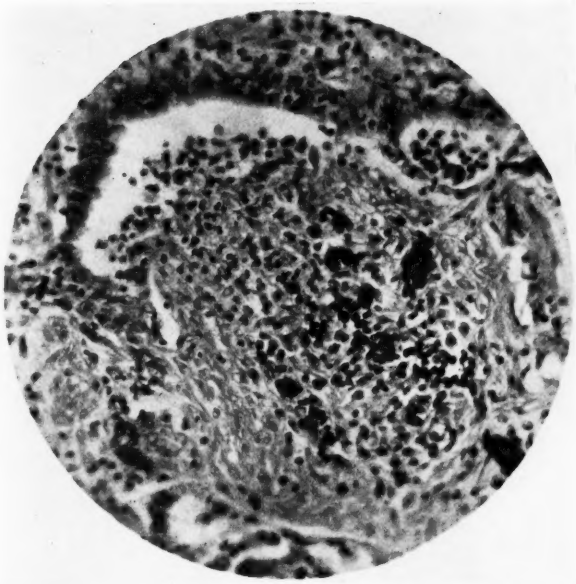

Fig. 24.—Higher power photomicrograph of bronchiole in Fig. 23. Plug of granulation tissue nearly filling the lumen, capillaries congested. On one side epithelium is beginning to cover the granulation tissue. Few well-preserved polymorphonuclear leukocytes in lumen. (× 400.)

Discussion.—The presence of a diffuse inflammatory process, subacute in nature, occurring in the lungs of a debilitated boy, suggested the possibility of pulmonary tuberculosis, although the preceding history of whooping-cough indicated a probable diagnosis of bronchopneumonia.

The pathologic picture in this case represents a somewhat more advanced stage of the lesion than that in Case I, since the organizing process, though confined to the lower lobes, is more extensive, involving now not only the bronchioles but also the adjacent collapsed alveoli. This more extensive lesion was made possible by the fairly normal condition of the left upper lung which permitted life to continue for a longer period of time than would have been possible had the process been uniformly scattered throughout all lobes as in the former case.

This case is of considerable interest from the etiologic point of view since measles and whooping-cough were the pre-existing infectious processes. A somewhat similar case was reported by Hart,[8] in which, following measles, both bronchiolitis fibrosa obliterans and bronchiectasis were observed.

Case III.—*History.*—The patient, E. F., was a man of forty-six who entered the hospital, February 1, 1926, complaining of shortness of breath and "asthma" of two and a half years' duration. The family history, past history, and social history were unimportant in relation to his illness, except that he had had influenza nine years before admission. His present illness began two and a half years before admission when he was first troubled by attacks of dyspnea. He was informed by a physician, at that time, that he probably was suffering from pulmonary tuberculosis, although repeated examination of the sputum failed to reveal acid-fast organisms. About one year before entry he had an exacerbation of bronchitis accompanied by fever, but again the sputum examination was negative for tubercle bacilli. Six months before entry to this hospital he was sent to a tuberculosis sanitarium, but again both *x*-ray and sputum examinations failed to substantiate the diagnosis. His weight had remained practically unchanged until five months before entry, when it began to diminish. Because of continued weakness, dyspnea, and "asthmatic attacks," he was advised to enter the hospital.

Physical examination showed a well-developed but emaciated man sitting up in bed, dyspneic, but conscious and rational. The chest was of the emphysematous, voluminous type with ribs and supraclavicular fossæ prominent. Expiration was everywhere prolonged and was accompanied by medium moist râles. The percussion note was dull over both apices, but hyperresonant elsewhere. The tactile fremitus was normal. The cardiac area was apparently within normal limits by percussion, but the apex impulse was neither visible nor palpable. The sounds were regular but faint, being obscured by râles and noisy breathing. The peripheral vessels were sclerosed, tortuous, and prominent. There were no signs of congestive failure.

The blood-pressure was 110 mm. systolic, 75 mm. diastolic. The temperature was 99.6° F., the pulse-rate 110, the respiratory rate 28. The white blood-cell count was 10,600 per cubic millimeter. The urine showed no abnormal elements. The Wassermann reaction was negative. During his stay in the hospital the patient showed a slight rise in temperature in the afternoon of 99.2° to 99.8° F. accompanied by a pulse-rate of from 92 to 120. An *x*-ray examination of the lungs was reported as showing "infiltration of both lung fields with tuberculosis." An examination taken two weeks later was likewise reported as indicating "generalized infiltration of both lungs, dilated bronchi in the lower right chest. Probably old tuberculosis with bronchiectasis."

In spite of all therapeutic measures the patient lost strength and weight, his temperature became more elevated in the afternoons, and he finally died March 12, 1926. Ten examinations of the sputum had been negative for tubercle bacilli.

The clinical diagnosis was pulmonary tuberculosis.

Autopsy Report.—*Gross Pathology.*—Inspection of the lungs showed general emphysema of the parenchyma with some local interstitial emphysema. In the upper lobe of the left lung and in the middle lobe of the right lung there were two large areas, each about 6 cm. in diameter, which were dark red, very firm, airless, and sharply demarcated from the surrounding tissue.

Microscopic Pathology.—Unfortunately the only tissue saved from these lungs was taken from the firm areas in which an organizing pneumonia was a prominent feature. Examination of the bronchioles, however, revealed ragged necrotic walls from which newly formed connective tissue could be seen extending out into the lumina, leading to partial or complete obliteration. Many bronchioles contained merely an acute inflammatory exudate, while others showed a chronic inflammatory reaction in their walls characterized by a dense infiltration of lymphocytes, endothelial leukocytes, and a few polymorphonuclear leukocytes, together with an increase in the connective-tissue elements.

Microscopic Diagnosis.—*Bronchiolitis fibrosa obliterans. Organizing bronchopneumonia.*

Discussion.—In this case the clinical similarity of bronchiolitis fibrosa obliterans and pulmonary tuberculosis is attested by the diagnosis of pulmonary tuberculosis by several physicians, by the fact that the patient was actually sent to a tuberculosis sanitarium, by the *x*-ray examination, and lastly by the clinical course. The prolonged clinical course and the presence of pulmonary emphysema may be attributed to the partial obliteration of many of the bronchioles still permitting the entrance of air into the alveoli. Inspiration being an active process draws the air past the obstruction, whereas on expiration only a portion of it is expelled. This valve action maintains the alveoli in a state of distention and probably leads, by rupture of their walls, to the interstitial emphysema observed in this instance at autopsy.

The etiology of this patient's condition may well have been the attack of influenza which he suffered some nine years previously. That influenza frequently gives rise to such a pathologic process is evidenced by the lesions described by Winternitz.[9] It is interesting in this connection that in a similar case reported by Jochmann and Moltrecht[3] an "influenza-like bacillus" (Bac. pertussis Eppendorf) was seen in both the sputum and the prepared sections.

Case IV.—*History.*—The patient, P. D., was a man of seventy-three who entered the hospital, April 14, 1926, complaining of shortness of breath and a feeling of suffocation two weeks in duration. Two weeks before entrance the patient was troubled by a dry, hacking cough, with occasional exacerbations of "asthmatic attacks."

Physical examination showed the chest emphysematous in type and the expansion equal on both sides. Tactile fremitus was normal, the percussion note somewhat hyperresonant, and the expiratory phase of the breath-sounds was prolonged and accompanied by sibilant and squeaking râles. The temperature was 98.6° F. with a terminal rise to 100° F., the pulse-rate was 75 to 95. The respiratory rate was 25 to 30 until before death, when it rose to 40. The blood-pressure was 122 mm. systolic and 55 mm. diastolic. The urine contained 2 per cent. of sugar on several occasions. In spite of therapeutic measures the patient lost in weight and strength and died one week following admission.

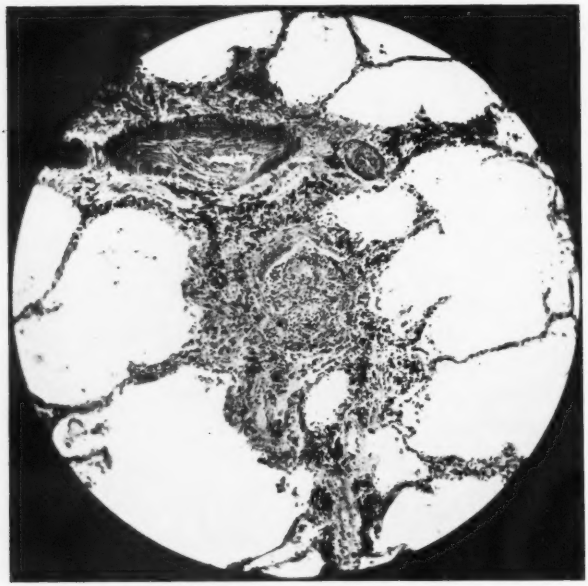

Fig. 25.—Low-power photomicrograph showing a small bronchiole, almost completely filled with granulation tissue. A portion of bronchiolar epithelium is present. Little fibrosis and phagocyted carbon pigment in peribronchiolar tissue. Alveolar emphysema in adjacent alveoli.

The clinical diagnoses were bronchopneumonia, bronchial asthma, arteriosclerosis.

Autopsy Report.—*Gross Pathology.*—The lungs were congested in the dependent portions. A purulent exudate exuded from the small bronchi. Small, firm, red areas were scattered throughout the lower lobes of both lungs, giving them a shotty feeling.

The gross diagnosis was bronchopneumonia.

Microscopic Pathology.—In some of the smaller bronchioles only a remnant of normal epithelium was present; the walls were scarred and the lumina were almost completely obliterated by plugs of granulation tissue growing in from the damaged wall. In several bronchioles elongated narrow epithelial cells, continuous with the normal epithelium, could be seen growing in and partially covering the fibrous tissue plugs in an attempt to reline the narrowed

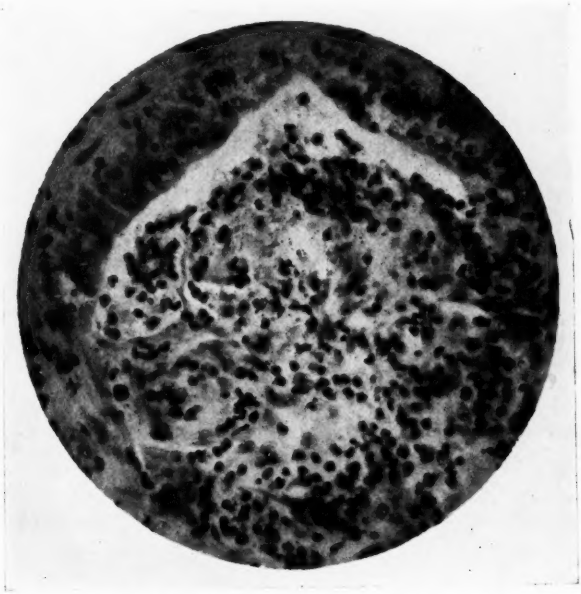

Fig. 26.—A higher power photomicrograph of the bronchiole in Fig. 25. Both capillaries and fibroblasts are visible in the granulation tissue plug. The lumen is greatly reduced in size and contains few polymorphonuclear leukocytes. (× 400.)

lumina. The large bronchioles showed a minimal inflammatory reaction in that the epithelium was intact and the lumen contained an exudate composed of precipitated albumin and well-preserved polymorphonuclear leukocytes. The alveoli showed no reaction, but were thin walled and unusually dilated (Figs. 25, 26).

Microscopic Diagnosis.—*Bronchiolitis fibrosa obliterans. Alveolar emphysema.*

Discussion.—The conspicuous progression of symptoms with dyspnea required consideration of a possible underlying tuberculous lesion. In this patient the partial obliteration of the bronchioles may well have been the important factor in the production of the alveolar emphysema. This case is very similar to those cases of bronchiolitis obliterans in elderly subjects reported by Müller.[7]

Case V.—*History.*—The patient, F. A., was a man of forty-two who entered the hospital, January 31, 1927, complaining of shortness of breath and cough two weeks in duration. His past history showed that three years previously he had had influenza and since that time had never been entirely well, having always been bothered by "bronchitis." He had been at another hospital a year before for two or three months because of "pneumonia." He had occasionally been troubled by bronchial wheezing, especially when lying down.

His illness had begun two weeks before entry, when he suffered chills, fever, and pain over the right lower ribs anterolaterally. He felt better after treatment in the Out-patient Department, but a week before admission noted an exacerbation of all symptoms and was forced, finally, to enter the hospital.

Physical examination showed dulness and numerous moist and crackling râles everywhere over the right lung except at the apex. The left lung showed no change in breath-sounds and only a few moist râles. During the following days the patient developed signs of consolidation of the left lung, and the *x*-ray report showed the "right side contracted, the left lung field dense, the heart pulled to the right. Impression: Tuberculous pneumonia or old empyema. Infiltration of left apex consistent with tuberculosis."

The clinical diagnosis was pneumonia, probably tuberculous.

Autopsy Report.—*Gross Pathology.*—The right lung and an area in the upper lobe of the left lung were firm, gray, and rubbery. Purulent material exuded from the bronchi. There was a small abscess at the base of the right upper lobe. The remaining lung tissue was soft and crepitant with questional areas of recent bronchopneumonia.

The gross pathologic diagnosis was diffuse organizing pneumonia with abscess.

Microscopic Pathology.—All sections were taken from an area of organized pneumonia showing the alveoli and bronchioles distorted, partially collapsed and filled with fibrous tissue. The pleura was greatly thickened and in one area showed a recent inflammatory exudate superimposed on an old organized pleuritis.

Microscopic Diagnosis.—*Organized pneumonia. Bronchiolitis fibrosa obliterans.*

Discussion.—The findings in this case are consistent with either an organized pneumonia or the end-result of a lesion which primarily injured the bronchioles, producing bronchiolitis fibrosis obliterans. This case is included because we believe that some cases, such as this, of so-called diffuse organizing bronchopneumonia represent the final stages of bronchiolitis fibrosa obliterans that have not gone on to recovery. This observation is not original with us, for many years ago both Ribbert[11] and Herbig[12] observed that the proliferating connective tissue in some cases of so-called indurating or organizing pneumonia began, primarily, with the organization of fibrin within the lumen of the bronchioles by the fibroblasts of the bronchiolar walls. Aldinger,[4] Wegelin,[5] and Fraenkel[10] likewise subscribed to this view. It is, of course, well recognized that, in most cases of organizing pneumonia, organization of the fibrin begins in the alveolar spaces by the fibroblasts of the alveolar walls.

The etiology, as in the former case, may possibly be traced to influenza which occurred three years previous to his entry into the hospital

Summary.—Bronchiolitis fibrosa obliterans is a well-defined clinical and pathologic entity first described by Lange in 1901, and since recognized by A. Fraenkel, Friedrich Müller, and other authorities. In this communication we have presented one case showing the lesions in their purest form involving the bronchioles but not the alveoli or larger bronchi. The sequelæ of the disease have been illustrated by 4 cases showing extension of the fibrosing process to the alveoli, but with predominant injury demonstrable in the bronchiole. Clinically and by gross inspection pathologically, the lesions simulate miliary tuberculosis. The differentiating criteria have been enumerated.

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CLINIC OF DRS. ROBERT S. PALMER AND HOWARD B. SPRAGUE

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FOUR CASES ILLUSTRATING THE UNTOWARD SYMPTOMS WHICH MAY BE PRODUCED BY THE USE OF POTASSIUM SULPHOCYANATE IN THE TREATMENT OF HYPERTENSION

THE recent paper of Gager has reawakened interest in the use of sulphocyanate in the treatment of hypertension. He found the potassium salt effective in reducing many abnormally high blood-pressures when given in the following dosage: $1\frac{1}{2}$ grains three times daily for one week, twice daily for the second week, and once daily for the third week. The drug may be continued at the last dosage less frequently, or may be given in higher dosage, depending on the effect. Gager briefly reviewed the literature on sulphocyanate therapy.

Nichols in 1925 published a very complete discussion of the sulphocyanates, with a review of the literature since the introduction of this drug into therapeutics by Pauli in 1903. Nichols showed that the toxic effects of lethal doses in animals are: (1) To abolish muscular activity; (2) to stop the heart; (3) to cause a rise in blood-pressure if not immediately fatal; (4) to cause diarrhea in dogs; (5) to produce diuresis in rabbits; and (6) in the final stages of poisoning to produce intense irritation of the motor cells of the spinal cord. However, the minimal lethal dose for the average 150-pound man is 15 to 30 gm., whereas the therapeutic dose is 15 grains per day.

This author used the sodium salt, 5 grains, in 1 dram of water three times a day for a week, twice a day for a week, and once a day thereafter, varying the dosage to suit the case. He

reported very good results. Disagreeable symptoms noted by him were nausea and nervous disturbances.

The sulphocyanates have been widely used and usually with especial success in the variable type of hypertension as reported, for instance, by Lörcher and Askanazy.

Whether or not it is desirable to reduce hypertension when one is able to do so is an open question at any time. Certainly it is not desirable, for instance, in chronic nephritis with hypertension. We are presenting four patients with essential hypertension in whom reduction of blood-pressure has been attended with untoward symptoms suggesting that the hypertension is a favorable reaction in the part of the organism and that it should be maintained rather than lowered in these cases.

Case I.—J. B., a married Italian-American barber of forty-eight, whose family and past histories were negative, was known to have had hypertension

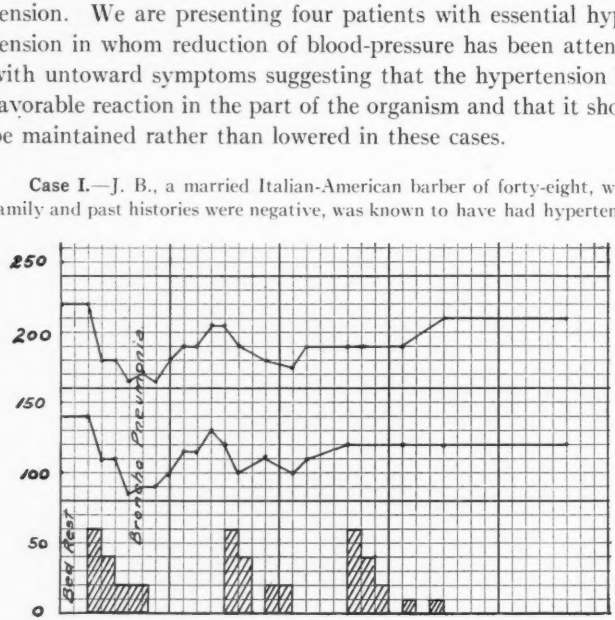

Fig. 27.—In this and the following figures each ordinate marks off one week except where dotted lines indicate the lapse of several months. The abscissæ represent the blood-pressure in millimeters of mercury, the upper tracing showing the systolic, the lower tracing showing the diastolic. From the base line every two divisions stands for $1\frac{1}{2}$ grains of potassium sulphocyanate. For instance, the first course of treatment indicated in Fig. 27 is $4\frac{1}{2}$ grains per day for one week, 3 grains per day for one week, and $1\frac{1}{2}$ grains per day for one week and a half. See text for further discussion of the figures.

for several years. Three years before starting potassium sulphocyanate therapy the systolic pressure was 205 mm. of mercury, the diastolic 135. The

urine at that time showed albumin and rare hyaline casts. The non-protein nitrogen was 30 mg. per 100 c.c. of blood.

The patient had always been a hard worker, a heavy eater, and an obese man. He suffered many respiratory infections and had been ill with bronchopneumonia twice.

Dyspnea on exertion growing worse in the two months preceding his last entry into the Massachusetts General Hospital and substernal distress on exertion brought him in for the third time. Urine examination again showed a slight trace of albumin and occasional casts. Non-protein nitrogen and phenolsulphonephthalein tests were normal. The heart was found considerably enlarged both by physical and roentgen-ray examination. There was a diastolic gallop rhythm. Blood-pressure was 210 systolic and 140 diastolic after eight days in bed. Alternation of the pulse was found.

Potassium sulphocyanate was then started with the results indicated in Fig. 27. An immediate and definite drop in both systolic and diastolic pressures was obtained. When the drug was omitted, these pressures rose again. A second course produced the same effect. The interesting thing is that this patient felt better when not taking the drug. He complained of vague weakness and loss of strength during its administration and found relief from this feeling when it was omitted.

The patient has continued to improve clinically. He has been digitalized and has been on a reducing diet. Diagnosis: Hypertensive and probably arteriosclerotic heart disease. Essential hypertension or chronic nephritis with hypertension. Angina pectoris.

Case II.—J. H. C., a single native, retired grocer of sixty-four, whose family and past histories were irrelevant, entered the hospital complaining of

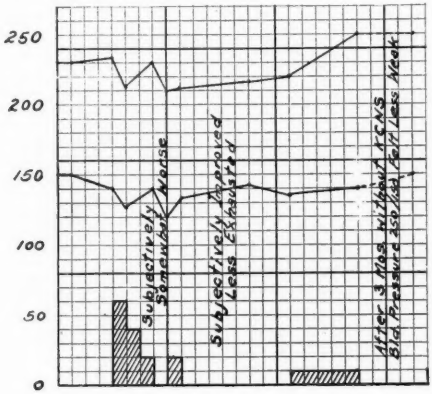

Fig. 28.—Case II.

occasional sharp precordial pain on exertion for twenty years. For ten years he had noticed gradually progressing dyspnea on exertion. For six months

attacks of dyspnea had been awakening him at night once a week. For two days before entrance he had been coughing up blood. The features of the physical examination were obesity, broad supracardiac dulness, hypertrophy of the heart, absolutely irregular pulse, a few moist râles at the lung bases, absence of edema, and a blood-pressure of 230 mm. mercury systolic and 170 mm. diastolic.

The urine showed a large trace to a slight trace of albumin, and occasional hyaline and brown granular casts. The phenolsulphonephthalein test was 25 per cent., the non-protein nitrogen was 37 to 59 mg. per 100 c.c. of blood.

The patient was improved by two and a half weeks' rest in bed, at the end of which period his blood-pressure was 230 mm. mercury systolic and 130 mm. diastolic.

After discharge potassium sulphocyanate was administered with some reducing effect as shown in Fig. 28. This patient at first felt somewhat better when taking the drug, but finally reached the same conclusion as did the first patient, namely, that he felt stronger when not taking it.

Diagnosis: Arteriosclerotic and hypertensive heart disease. "Arteriosclerotic" chronic nephritis. Auricular fibrillation. Cardiac asthma.

Case III.—L. M. M., a white married housewife of forty-three, whose family and past histories were essentially negative, was known to have had a

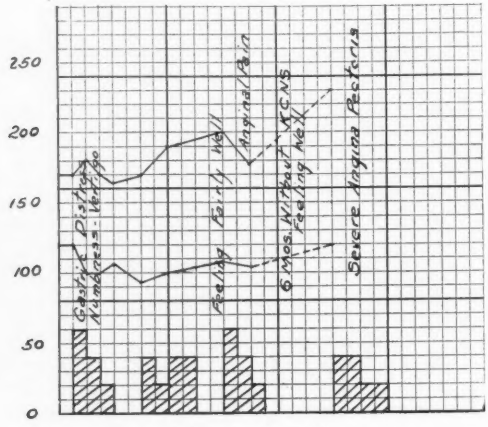

Fig. 29.—Case III.

blood-pressure of 160 to 180 systolic for five years. She complained chiefly of exhaustion without definite symptoms.

Physical examination and *x*-ray study of the heart showed enlargement of the "rheumatic" shape and characteristic aortic and mitral diastolic murmurs.

Diagnosis: Essential hypertension, probably related to the menopause. Rheumatic heart disease, aortic regurgitation, and mitral stenosis.

Figure 29 shows the course of the systolic and diastolic pressures and the amounts of sulphocyanate given. At first, with a slight fall in pressure, the patient felt better. However, she had definite, though slight, attacks of angina pectoris during the first course of treatment and again during the third course, while during the six months without treatment she was free from angina. Finally, after less than a week of the fourth course, she had three attacks of pain in the left chest. She was not seen during or after these attacks.

Case IV.—L. M. D., a single school teacher of sixty-nine, was known to have had a systolic blood-pressure of 160 a few months before examination. Two months before she was seen for the first time she had suffered two

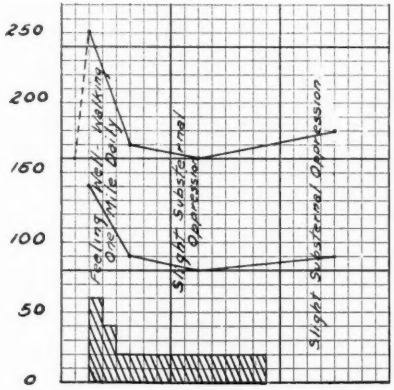

Fig. 30.—Case IV.

moderately severe nosebleeds and there was a question of heat stroke. Her complaints were fatigue, some giddiness, and tinnitus in the left ear. Her father died at sixty-three of heart trouble; her mother died at seventy-three from a cerebral accident. The past history was not remarkable.

The blood-pressure was 240 systolic and 140 diastolic. The heart was slightly enlarged.

Diagnosis: Arteriosclerotic and hypertensive heart disease.

With some limitation of her life and with the use of potassium sulphocyanate, as indicated in Fig. 30, the patient felt well except for slight substernal oppression on exertion such as walking. There was apparently marked effect from the drug in reducing the blood-pressure and this was accompanied by mild angina pectoris.

Discussion.—In these four patients we have found cases unsuited to sulphocyanate therapy. The first two complained

chiefly of weakness when on the drug. When the drug was omitted this symptom was relieved. The explanation of this symptom in terms of physiology is not clear and in any event is theoretical. It is reasonable to suppose, however, that in these patients there was need in certain organs, such as the kidney, brain, or possibly the adrenals, for a constant tension well above the average. The unaccustomed lowering, when it occurred, was represented by a feeling of weakness.

The last two patients complained of severe and mild angina pectoris respectively when on the drug; the third patient being definitely relieved of this symptom when the drug was discontinued. The reasonable explanation in these two patients is that the coronary arteries, somewhat narrowed by sclerosis, required a certain increased pressure to maintain an adequate blood-supply to the myocardium. With a lowering of blood-pressure this supply was decreased with resulting anemia of the myocardium and angina.

Summary.—Four cases are presented illustrating the symptoms that may be produced in certain patients by the use of potassium sulphocyanate for reducing blood-pressure. In two patients the drug caused uncomfortable weakness. In two patients the drug appeared to produce angina pectoris. The symptoms in the patients here reported seem to have been due to the lowering of the blood-pressure rather than to any toxic effect of the drug, which is in many instances a useful therapeutic agent.

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CLINIC OF DR. FREDERICK C. IRVING

BOSTON

THE TREATMENT OF ECLAMPSIA

ECLAMPSIA is a disease peculiar to the pregnant, parturient, or puerperal woman. It is characterized by convulsions, coma, or both. The condition is due in theory to a hypothetic toxin whose nature and site of origin are at present unknown.

Until comparatively recent years the generally accepted treatment of eclampsia was immediate evacuation of the uterus. Such therapy was based on the assumption that since none but childbearing women had the disease the product of conception must be the source of the poison. Accouchement forcé was advocated by some, induction of labor by others, while those who believed in cutting the Gordian knot found in cesarean section the sword of Alexander. However, as time went on it became apparent that the maternal death-rate in cases treated by artificial delivery was unnecessarily high. A mortality of about 25 per cent. was to be expected among eclamptics delivered by dilatation and extraction or by the induction of labor, while the proportion of such women who died following cesarean section was even greater. It seemed that a certain number lost their lives as the result of the measures undertaken to save them. Believing this to be the case, Strogonoff in 1897 attacked the problem from a different angle. He believed that whatever might be the cause of eclampsia the convulsions themselves were often induced by various external stimuli, such as operative procedures, examinations, or even the administration of a hypodermic injection. He put his patients in a darkened room, disturbed them as little as possible and kept them in a semi-

somnolent condition by the use of morphin and chloral given at regular intervals according to a definite routine. Any manipulation, even so slight as subcutaneous medication, was preceded by light chloroform narcosis. If the patient had more than three convulsions after entering the clinic a venesection not exceeding 400 c.c. was done. No operative delivery was permitted unless the fetus was in danger. Strogonoff's experience as reviewed by Stander covered 799 cases in the period from 1897 to 1924. Eliminating the patients treated in the early years before the method was perfected and those in whom it was not properly carried out Stander selected 210 eclamptics treated according to the Strogonoff régime with a mortality of 3.3 per cent., which, taken at its face value, is a brilliant showing. A more careful analysis, however, revealed that there were other factors than the treatment which contributed to the low mortality. It was Stander's opinion that the type of eclampsia treated in Strogonoff's clinic was comparatively mild. About 70 per cent. of his cases had no convulsions before entering the clinic. Since we believe that modern prenatal care has made eclampsia almost a preventable disease it is at once evident that Strogonoff's prophylaxis falls far behind his treatment. Moreover, 50 per cent. of his cases had only one convulsion. Inasmuch as it is an established fact that the gravity of the condition is greatly increased by the number of the convulsions, it is evident that most of Strogonoff's cases represented a much less virulent type than that seen in American lying-in hospitals, where many patients are sent in after having had many fits and with little or no prenatal care.

For the past forty years the Rotunda Hospital in Dublin has been a consistent advocate of the conservative treatment of eclampsia. The emphasis there has been placed on the use of morphin in repeated doses and thorough evacuation of the gastrointestinal tract rather than on the employment of chloral and chloroform. Lately Lazard of Los Angeles has reported good results from intravenous administration of magnesium sulphate. Some experience with this drug has led me to believe that by its use the convulsions may be controlled in the majority of cases,

but that in spite of this a considerable number of eclamptics so treated will die. In general, the present trend in the management of the convulsive toxemia of pregnancy is toward conservatism. One treats the disease and disregards the pregnancy. Wilson has found that twice as good results were obtained at the Johns Hopkins Hospital in ante- and intra-partum eclampsia when conservative methods were substituted for radical. In spite of a growing improvement it seems unlikely, however, that the lives of some eclamptics can be saved by any method of treatment at present in use. Judging by the clinical course of the disease in some individuals and by the extent of the liver lesions found at autopsy it would appear that in spite of what we believe to be intelligent treatment they are headed for dissolution before they enter the hospital. Our aim, therefore, should be to prevent eclampsia by systematic prenatal care which will enable us by routine blood-pressure observations, urinalysis, and history taking to detect the pre-eclamptic state. If after rest in bed, salt poor low protein diet, and vigorous saline catharsis no improvement is evident pregnancy should be terminated by the most appropriate means. In this way not only will the occurrence of convulsions in patients under observation become rare indeed, but the danger of a resulting nephritis will be reduced to a minimum. Faced with actual convulsive seizures the physician will greatly increase his patient's chances of recovery if he refrains from emptying the uterus and adopts a conservative policy of treatment.

The conservative methods outlined above, those of Strogonoff, Lazard, and the Rotunda school, may be called symptomatic in that they are directed against the main feature of the disease, namely, the convulsions. At the Boston Lying-in Hospital it has seemed to us that it would be more logical to remove from the circulating blood a certain amount of the hypothetic toxin which we believe to be the cause of the condition. Venesection has been employed in eclampsia for many years either alone or in combination with other methods. Against postpartum convulsions it has always been the heaviest piece of artillery. Unfortunately, if enough blood is withdrawn to produce a beneficial

effect, anemia, debility, and lack of resistance to infection are likely to follow. In all diseases where a definite toxin has been demonstrated it has been found that this poisonous agent was transported in the blood-plasma and not in combination with the corpuscles. The problem, therefore, became a search for a method whereby we might bleed the patient of a certain amount of her plasma without the loss of her corpuscles. Abel, Rowntree, and Turner found that using an anticoagulant they could bleed normal dogs in fairly large amounts, separate the corpuscles from the plasma by centrifugalization and after washing the red cells in Locke's solution return them to the animals in the same physiologic fluid. They were able to repeat this process until they had removed all the plasma in the circulating blood. Their dogs showed no ill effects: they behaved as healthy animals. They called this process *plasmaphæresis*.

Removing a smaller proportionate amount of plasma Carstens of Detroit and Brittingham, O'Hare and Drinker of Boston have treated a small number of chronic nephritics in a similar manner. Since the kidney damage in chronic nephritis is permanent a cure could not have been expected in any case, although symptomatic improvement was noted in some. Eclampsia, on the other hand, seems to be a suitable disease for such a procedure since it is an acute condition and the patient is either dead or on the road to recovery in a comparatively short time. If we assume that the body of an eclamptic of average size contains about 5 liters of blood and we remove the plasma contained in 1 liter we have diminished the toxin in the circulation by 20 per cent. Should the convulsions cease, the sensorium clear, the output of urine increase, and the blood-pressure fall, no further steps would be necessary. If satisfactory improvement did not follow we would be in a position to remove the plasma contained in a second liter because we would have restored the corpuscles belonging to the first 1000 c.c.

As an example of how we have carried this method into effect at the Boston Lying-in Hospital and as a clinical picture of eclampsia so treated I wish to present the case of Mrs. D. M., admission No. 38,887.

She is an Italian housewife, forty-one years old, in the thirty-fifth week of her seventh pregnancy. Her children at birth have varied in weight from 6 to 9 pounds; all are living and well except the second which died at four years and the last which was stillborn. There have been no miscarriages. All pregnancies, labors, and puerperia have been normal except the last which was complicated by a postpartum femoral phlebitis. The past medical and surgical histories are negative.

Mrs. D. M. first applied for treatment at the pregnancy clinic of the Boston Lying-in Hospital on November 21, 1927. Her physical examination was negative save for a justo-major pelvis. Her systolic blood-pressure was 138 and her urine contained a heavy trace of albumin. On this account and because of severe dyspnea she was at once admitted to the hospital. The day after entrance the one-hour renal test showed the specific gravity of the urine to be fixed. The chemical examination of the blood revealed a non-protein nitrogen of 20, a urea nitrogen of 9.1, a uric acid of 5, a blood-sugar of 95, and chlorids of 519. She weighed 294½ pounds, the abdomen and lower extremities were very edematous and there were a few moist râles at the bases of both lungs. The fetal heart was not heard. She was put to bed, placed on a salt poor low protein diet and given 1 ounce of saturated magnesium sulphate solution by mouth every hour up to the point of free watery catharsis (twelve to fourteen bowel movements a day).

In spite of this treatment from November 21st, the day of admission, to November 25th the blood-pressure rose steadily from 140/110 to 178/110, although the albumin in the urine somewhat decreased. On the morning of November 25th the membranes ruptured spontaneously and she started in labor. Soon afterward a convulsion occurred, followed by a period of coma which lasted fifteen minutes. Labor then terminated by the normal delivery of a stillborn fetus weighing 4 pounds, 7½ ounces. At this time 2 ounces of very bloody urine were obtained by catheter. It was decided to do a plasmaphæresis. While preparations were being made another convulsion ensued which was controlled by chloroform. By this time the edema of the lungs had become marked, the cyanosis was intense, and the respirations stertorous.

Bleeding.—The glassware used in the procedure I am about to describe is autoclaved and always kept ready for use. Sphygmomanometer cuffs were applied to both arms. The one on the right arm was used for frequent blood-pressure observations, the one on the left as a tourniquet for venous compression. The left median basilic vein was exposed under novocain anesthesia and opened by a small transverse incision. A cannula connected to a short piece of rubber tubing was inserted into the vein and 1000 c.c. of blood was allowed to run into a sterile glass graduate in which enough sodium citrate solution to prevent clotting had been placed. While the blood was running in, it was thoroughly mixed with the citrate by stirring with a glass rod. The pressure in the tourniquet was now reduced to zero and special smooth-faced bull-dog clips were applied above and below the incision in the vein for temporary occlusion.

Centrifugalization.—The citrated blood was divided among four 500-c.c. centrifuge bottles so that each contained about 250 c.c. The two bottles of each pair that were to be placed opposite each other in the centrifuge head

were balanced on a torsion balance. Any deficiency in weight was made up by adding blood or salt solution to the lighter of the two. The purpose of this was to insure smoothness in the operation of the machine. All four bottles were covered with sterile paper caps and placed in the centrifuge, which was run at 5000 revolutions per minute for twenty minutes. At the end of this time the bottles were removed and the supernatant plasma siphoned off under

Fig. 31.—Blood-pressure chart during plasmaphæresis.

sterile conditions into a flash, leaving the corpuscles behind in the remaining plasma in which they were suspended. To accomplish this the long end of the siphon was passed through one hole of the two-hole stopper closing the flask, and a short glass tube fitted with a piece of rubber tubing was passed through the other hole to be used as a sucker for starting the siphon.

Washing the Corpuscles.—To the corpuscles remaining in each bottle enough normal saline solution was added to bring the amount in each up

to about 250 c.c. Each bottle was again balanced against its fellow of the opposite side, the paper caps applied as before, and the corpuscles diffused into the salt solution by gently rotating them. They were again centrifuged at the same rate of speed for twenty minutes. The supernatant solution was siphoned off as before. The purpose of this procedure was to wash the corpuscles once and thereby remove the bulk of the remaining plasma in which they had been suspended after the original centrifugalization.

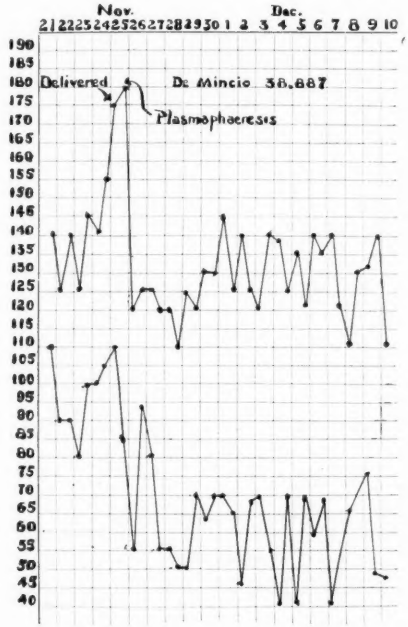

Fig. 32.—Bidaily blood-pressure chart.

Reinfusion of Corpuscles.—The corpuscles remaining in all four bottles were then made up to about 1 liter with normal salt solution and reinfused into the patient in an ordinary transfusion flask.

In Fig. 31 are shown the changes in blood-pressure during and after the bleeding and reinfusion of washed corpuscles.

Coincidently with the first convulsion the patient was started on the Strogonoff régime. She was given morphin, gr. $\frac{1}{4}$, subcutaneously at 7.20 P. M. November 25th, chloral hydrate, gr. 30, by rectum at 8.30 P. M., morphin, gr. $\frac{1}{4}$, at 11.15 P. M., chloral hydrate, gr. 30, at 2.00 A. M. November 26th, chloral hydrate, gr. 20 at 8.00 A. M.

The patient made an uninterrupted convalescence. Her bidaily blood-pressure is shown in Fig. 32. At the time of discharge, the fourteenth day postpartum, the blood-pressure was 110/48, the urine free of albumin, and the one-hour renal test showed no fixation of specific gravity. On the several occasions when she was seen in the toxemia clinic after leaving the hospital her blood-pressure and urinary findings were as follows:

Date.	Blood-pressure.	Albuminuria.
January 6, 1928	128/60	None
February 13, 1928	108/60	"
March 16, 1928	98/60	"
July 7, 1928	146/100	"
November 2, 1928	104/72	"

Apparently, therefore, in so far as blood-pressure observations and urinalyses may be accepted as criteria, no permanent damage had been done to her kidneys by the convulsive toxemia.

Up to the present time plasmaphæresis has been performed eighteen times on fifteen patients. In 5 eclamptics prompt recovery followed. In 5 cases of pre-eclamptic toxemia where other methods, including induction of labor, had failed to produce a beneficial result a reduction of the blood-pressure and the disappearance of albuminuria ensued. Five chronic nephritides so treated have shown only temporary improvement, although there was disappearance of edema and increase in the urinary output. Where red counts have been done, the number of erythrocytes has shown little or no diminution following this method of treatment. Since the number of cases treated, particularly those of eclampsia, has been small, this should be regarded merely as a preliminary report. We make no claim that this is the best way to treat eclampsia. We believe that the method is logical and it is our hope that other investigators may be led to employ it on their own account.

CLINIC OF DRS. HARRY LINENTHAL AND MAURICE E. BARRON

BETH ISRAEL HOSPITAL

THROMBO-ANGIITIS OBLITERANS—A GENERALIZED VASCULAR DISEASE

THROMBO-ANGIITIS obliterans since its first description by Winiwater some fifty years ago under the name of "endarteritis obliterans," and the establishment of the disease as a clinical and pathologic entity by the classic studies of Buerger in 1910, is referred to and defined in text-books as a disease involving the deep arteries and veins and the superficial veins of the extremities. The disease is characterized pathologically by the slow formation of a thrombus. Starting from the intima of the vessel, this thrombus undergoes organization and gradually causes a complete occlusion of the lumen of the vessel involved in the inflammatory process.

On the clinical side, thrombo-angiitis obliterans is characterized by a slow and insidious onset and development of many years' duration, manifesting itself first by intermittent attacks of pain when demand of muscular effort is made on the affected limb—the so-called "intermittent claudication"—and later by nutritional disturbances of the affected limb characterized by pain, rubor or cyanosis of the extremity, ischemia when the limb is raised above the horizontal, and finally by gangrene of the affected limb, usually requiring mutilating operations. Recognized as it is, that the disease is due to some systemic cause, though of obscure etiology, it is generally assumed that the disease involves only the blood-vessels of the extremities.

Dr. Barron, in a communication to the American College of Surgeons at the recent meeting in Boston, has directed attention,

from a study of cases of our own series and from a number of cases he collected from literature, some of which have reports of postmortem examinations, to the more general distribution of the disease which may attack the walls of the blood-vessels, both veins and arteries, throughout the vascular system and may involve not only the blood-vessels of the extremities but also the cranial, thoracic, coronary, and abdominal vessels. The clinical picture of the disease will be characterized according to the vessels involved, so that, for example, lesions affecting the arteries of the brain may give rise to hemiplegia of a varying degree of severity; or should the coronary vessels be involved, the characteristic symptoms of coronary thrombosis or angina pectoris may ensue.

The 2 cases we are going to present point, with a great degree of probability, to an involvement of the cerebral arteries by the same pathologic process which characterizes the disease in the vessels of the extremities.

Case I.—J. S., forty-eight years of age, a Russian Jewish storekeeper, came into the Beth Israel Hospital for the second time, complaining of a sudden onset of loss of motion and weakness of his right arm and leg, and some difficulty with his speech. He thought, at first, that the difficulty was due to some trouble with his right artificial leg which he was wearing since a previous amputation; but he soon found that he was unable to stand. He fell a number of times, and he noticed that his speech became very slow and thick.

Past History.—He gives a history that ten years ago he was operated upon for duodenal ulcer, at which time a gastro-enterostomy was done. His symptoms, however, were not relieved and six months later he was operated upon for gastrojejunal ulcer. Shortly after leaving the hospital after the second operation he began to complain of severe pain in the calf of his right leg on walking, and a more or less constant pain and numbness in the toes of his right foot. Three years later he developed gangrene of the third toe of the right foot. He was laid up at that time in a hospital in Boston for eleven weeks and his toe was finally amputated. The pain in his right leg and foot, however, continued and shortly after he developed gangrene of his second toe. The patient then entered the Beth Israel Hospital for the first time. A diagnosis of thrombo-angiitis obliterans was made and amputation below the knee was done. The stump seemed to heal well and he was sent home. Two months after his discharge from the hospital, while getting along fairly well with his artificial leg, he returned complaining of bleeding hemorrhoids. These bled so profusely that a severe secondary anemia developed and a transfusion was required. The hemorrhoids were removed

under local anesthesia. At that time he also began to complain of some pain, not very severe, in the calf of his left leg. Pulsation in the left dorsalis pedis was not felt. The patient got along quite well with his artificial right limb until the present illness which was of sudden onset.

Physical Examination.—At time of entrance the physical examination reveals a well-developed man of forty-eight, lying fairly comfortably in bed, co-operative, and rational. Speech seems somewhat thick and slurring. His mouth is pulled over slightly toward the left. His pupils are equal and react to light and distance. Throat is negative. Many of his teeth are missing; those remaining are in poor condition with a good deal of pyorrhea. Mucous membrane is of fair color, not cyanotic. Tongue is moist and protrudes in the median line. The tonsils are somewhat large and slightly reddened. His glands are not enlarged. Thyroid is normal.

There is cardiac dulness 9.5 cm. to left and 2 cm. to right of the mid-sternal line. Apex impulse is not seen, but is felt in the sixth interspace; no palpable thrill; sounds of good quality, regular and slow. There is a short blowing systolic murmur heard best at the apex and well transmitted to the axilla. Aortic second is greater than pulmonic second, but not accentuated. There is no enlarged area of supracardiac dulness. His lungs are resonant throughout. Breath-sounds are normal, except for slight prolonged high-pitched expiration over the right upper back. No râles are made out. His abdomen is negative except for a mid-epigastric scar of his previous surgical operation. His blood-vessels are palpable and are easily compressed. His blood-pressure is 114 systolic, 60 diastolic. His right knee-jerk is greater than the left. Abdominal reflexes not obtained. Cremasteric reflex is normal on the left; not obtained on the right. No Babinski, Gordon, or Oppenheim on the left. The grip of the left hand is much stronger than that of the right. Patient is unable to move the stump of his right leg. Rectal examination is negative; no hemorrhoids. The prostate is of normal size and consistency.

Laboratory Work.—Blood Wassermann negative. Non-protein nitrogen 33 mg. per 100 c.c. of blood. Blood-sugar 75 mg. per 100 c.c. of blood. Several urine examinations negative. On one occasion a rare hyaline cast was seen. Red count 5,520,000; hemoglobin 80 per cent.; white count 7000. Differential count not remarkable. Smear showed a very slight achromia. *x*-Ray of the teeth showed definite evidence of abscess formation at the roots of many teeth.

The diagnosis was, obviously, that of a hemiplegia probably due to cerebral thrombosis. The patient's progress in the hospital was very satisfactory. Within one month's time the power on his right side became much better. Patient is at the end of his sixth week stay in the hospital. He has regained almost his entire motion and, as you see, has only a very slight residual paresis of his right side.

We thus have here a man who gives a history of many vascular accidents: a duodenal and gastrojejunal ulcer, gangrene of his right leg because of thrombo-angiitis obliterans, profuse bleeding

hemorrhoids, and ending with a thrombosis of his cerebral vessels. While it is true that a patient suffering from thrombo-angiitis obliterans may have duodenal ulcer, gastrojejunal ulcer, bleeding piles, and thrombosis of his cerebral vessels, the question arises as to whether all these vascular accidents might not be due to one underlying condition. In the absence of any evidence of arteriosclerosis, cardiorenal disease, or hypertension it may be reasonable to suppose that there is a relation between his thrombo-angiitis obliterans of the lower extremity and the other vascular accidents that he suffered from at various times, particularly the cerebral thrombosis, and that the underlying pathology was probably the same. That his disease has not yet become quiescent is shown by the fact that during his stay in the hospital he began to complain of severe pain in the calf of his left leg, and that the dorsalis pedis and posterior tibial could not be palpated on the left side.

Case II.—M. G., forty-five years of age, Jewish, born in Russia, entered the Beth Israel Hospital on August 10, 1928 complaining of loss of power of his left arm and left leg and acute onset of dizziness. Four days previous to entrance, while walking in the street in Youngstown, Ohio, the patient suddenly felt a tingling sensation in the left arm and leg which lasted for a few minutes. About three-quarters of an hour later he completely lost the power of his left arm and leg, and fell. Patient was placed on a train and sent to his home in Boston, when he entered the hospital.

There is nothing of any special significance in the patient's family history or habits.

Past History.—About a year and a half ago patient began to complain of pain in the calves of both legs on walking. This pain was extremely severe in the right foot, particularly in the right great toe. Examination in one of the neighboring hospitals at that time showed that there was no pulsation in the dorsalis pedis artery on the right, but it was definitely felt on the left. There was also a great deal of redness and tenderness of the right toe. Patient was at that hospital for twelve weeks and a diagnosis of thrombo-angiitis obliterans was made. The pain in his foot was most excruciating and did not respond to any kind of treatment, including typhoid vaccine. He then began to develop ulceration of the great toe. Amputation of his leg was considered. Dr. Jason Mixter, however, did a lumbar sympathectomy on him. The second, third, and fourth right lumbar sympathetic ganglia were removed. This operation had a most brilliant result. The pain in his foot immediately stopped and the ulceration of his toe completely healed. He was discharged from the hospital feeling perfectly well. The dorsalis pedis on the right, however, could not be felt. A few months after he left the hospital he

developed a superficial phlebitis of his right leg which subsided with moderate rest. He soon resumed his work as a salesman until he was overtaken by his present illness.

Physical Examination.—At time of entrance the physical examination revealed a well-developed, well-nourished man, lying quietly in bed, not suffering from any great discomfort. His pupils are equal and react to light and distance. Ocular movements are normal. His teeth are in fair condition. His throat is negative. Tongue is clean. There are no enlarged glands. Thyroid is normal.

His chest is symmetrical, well developed, with normal respiratory excursions. The lungs are resonant throughout; normal vesicular breathing; no râles. The left border of cardiac dulness is 7½ cm. from the midsternal line. The right border of cardiac dulness is 2 cm. from the midsternal line; apex in fifth interspace in midclavicular line, sounds regular, of good quality, no murmurs. His blood-pressure is 110 systolic and 80 diastolic. His abdomen is negative. There is a complete paralysis of the left arm and leg; also a slight obliteration of the left nasolabial fold. All the reflexes, biceps, triceps, knee-jerks, and ankle-jerks are exaggerated on the left. Positive Hoffman's sign on the left but not on the right. Left ankle-clonus but no Babinski. Abdominal reflexes present on both sides. There are no sensory disturbances. Fundus examination showed considerable tortuosity of the veins which are rather dark in color and the arteries show a white line around the border.

Laboratory Work.—Blood Wassermann negative. Blood-sugar 102 mg. per 100 c.c. of blood. Repeated examinations of urine were negative. Red count 5,000,000; hemoglobin 100 per cent. There was nothing remarkable in the differential count. Smear showed no achromia. The platelets were normal.

The patient showed a very marked and rapid improvement of his paralysis. A few days after entrance to the hospital the motion of his arm and leg returned, so that two weeks after entrance he was able to walk. On August 30th the patient began to complain of pain in the right leg. Examination revealed a superficial phlebitis, which cleared up with rest. The patient, as you see him now, four weeks after admission, is able to walk and only shows a very slight residual paresis in his left arm and leg.

This man, likewise, shows no clinical evidence of arteriosclerosis or cardio-renal disease. He had definite thrombo-angiitis obliterans with two attacks of superficial phlebitis. He suddenly developed a complete hemiplegia which cleared up within a short time. This extremely rapid improvement could not have taken place if his hemiplegia were due to cerebral hemorrhage. It is interesting to note that while the gangliectomy improved the symptoms, it did not stop the progress of the disease, as is evidenced by the subsequent history.

This case, likewise, suggests that the vascular brain lesion from which the patient was suffering, was similar in character to that of the vascular disease in his legs and that his hemiplegia

was probably due to the partial occlusion with vascular spasm of his cerebral arteries rather than to a cerebral hemorrhage.

The two patients we have shown demonstrate that thrombo-angiitis obliterans may attack other parts of the vascular system besides vessels of the extremities. In these instances, in both of which thrombo-angiitis obliterans was definitely diagnosed, there was an involvement of the cerebral arteries which could not be explained on an arteriosclerotic basis and was, in all probability, due to the same pathologic process which was going on in the extremities.

The question might well be asked how to explain the fact that the disease manifests itself most commonly in the lower extremities, much less frequently in the upper extremities, and only very rarely in other parts of the vascular tree, so rarely as to have escaped general attention.

The probable reason that the characteristic signs and symptoms of thrombo-angiitis obliterans do not appear as frequently in the upper extremities, and only rarely in other parts of the body, may be looked for in the analogy to what takes place in extensive arteriosclerosis in the vascular tree, when on post-mortem examination one finds marked involvement of the vessels in the upper extremities and in the abdomen, yet we very seldom get arteriosclerotic gangrene in the upper extremities or gangrene of the abdominal viscera. The greater demand made on the circulatory channels of the lower extremities because of static conditions may favor the more rapid development of the lesion. Moreover, the feet are more susceptible to slight injuries from nail deformities and from calluses which are frequently the starting points of the gangrene which develops.

We know, moreover, that it is possible to maintain a sufficient circulation to keep up the nutrition balance of a part in the presence of occlusion of the main arterial trunk through collateral or anastomosing branches. If this is true for arteriosclerosis it is more so for thrombo-angiitis obliterans. For we know from the work of Meleney and Miller, of Lewis, and Lewis and Reichert, that collateral circulation and free anastomosis develop in inverse proportion to the extent and rapidity of the vascular

occlusion. For that reason, because the process of occlusion is slower and more gradual in thrombo-angiitis obliterans than in arteriosclerosis, there is a tendency to produce in this disease a more liberal collateral circulation.

It might be of interest at this time to compare the symptom-complex that occurs as a result of arteriosclerosis of the lower extremities and the same condition in the coronary vessels. The earliest symptoms in the lower extremities are usually intermittent claudication on walking a variable distance; the patient complains of severe cramp-like pains in the calves of his legs; he must stop and rest before he can continue. Later, there is occlusion of the peripheral vessels and possibly gangrene. A parallel syndrome occurs in sclerosis of the coronary arteries; the earliest symptom is a feeling of constriction through the chest or severe pain over the cardiac area. On exertion the patient must stop, if walking, and rest before continuing. The later manifestation of coronary sclerosis is a distinct narrowing of the lumen of these vessels or complete occlusion. In thrombo-angiitis obliterans the symptom-complex is likewise, first, partial occlusion and spasm of the vessel causing intermittent claudication and, later, complete occlusion.

The two cases shown point very definitely to the fact that a pathologic process similar to that which takes place in the extremities also occurs in the vessels of the brain. The same process may also involve the coronary vessels.

In the group of cases collected by Dr. Barron there are several cases of coronary thrombosis in young men suffering from thrombo-angiitis obliterans in whom there was not the slightest evidence of arteriosclerosis.

The question arises why do we not see more patients with coronary disease due to thrombo-angiitis obliterans and why the observation has not been made more frequently.

In view of the definitely established fact that the lesions of thrombo-angiitis obliterans do occur in the coronaries, as was shown by the reports of the postmortem findings in Dr. Barron's series, the suggestion is near at hand that the occasional cases of angina pectoris and coronary thrombosis that occur early in life,

without any evidence of vascular disease elsewhere, may, in some instances at least, be due to thrombo-angiitis obliterans of the coronaries and not to arteriosclerosis.

The reason that we do not find it more frequently on post-mortem examination may be due to the fact that the disease is characterized by a chronic course and that as years go on arteriosclerotic changes take place in the same vessels affected by thrombo-angiitis obliterans. The former lesion may be entirely overlooked in the presence of arteriosclerosis.

Summary.—Thrombo-angiitis obliterans is a general systemic disease which most frequently affects the blood-vessels of the extremities; but it is not, as is generally accepted, confined to those vessels. The disease may affect any part of the arterial tree, including the coronaries and cerebral vessels. The two cases we have shown, because of the absence of any arteriosclerotic basis for the cerebral vascular injuries, in all probability have the same pathology in the cerebral vessels as that in the vessels of their extremities.

CLINIC OF DR. LOUIS J. ULLIAN

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SUBACUTE BACTERIAL ENDOCARDITIS: DISCUSSION OF A CASE

Introduction.—When a diagnosis of this condition is established, one is at once confronted with the futility of any of the recommended therapeutic measures, and with this fact at hand it is easily understood why many such cases have only half-hearted attempts made at treatment and why so often nothing more than general hygienic care, good nursing, and absolute rest in bed is tried. It is probably true that these measures will in the end accomplish as much as any of the other therapeutic measures that may be employed. The disease is nearly 100 per cent. fatal even in cases where constant and varied attempts at therapy have been made. Recovery is reported only rarely and then we must assume that it has been spontaneous, for there is no evidence in these cases that the particular therapeutic measures used in any way affected the course of the disease. The rare case that may get well undoubtedly would go on to recovery with only hygienic care, nursing, and rest; and in mentioning possible recoveries we must bear in mind those cases where the diagnosis is suspected of being "endocarditis," but where no organism is demonstrable in the blood-stream and where the clinical course is not typical of malignant endocarditis. It is quite evident that if such a case is reported as a recovery we might reasonably question the diagnosis.

The case now presented has been of particular interest for the following reasons:

1. It has been possible to observe it very closely clinically.
2. There have been many of the classical complications.

3. The attempts at treatment have been constant and quite varied.

4. The diagnosis has been definitely established.

The patient, a single white girl of twenty-two, in her senior year at college, was first seen by the author on March 8, 1928, at which time the following history was obtained:

For approximately the past six weeks there has been some night sweating, a condition which never was present previously. During this entire period there was a continued loss of energy and she described herself as being "pepless." On closer questioning it was learned that since early January, 1928 she has had a loss of ambition, a definite listlessness, a loss of desire to keep up her studies, and as soon as her daily classes were over she desired to recline and do nothing but rest. No amusements held any interest; her appetite became poor, although she never ate heartily. About four weeks ago while in town the patient had a chilly spell and that night it seemed that she was "burning up." About this time she noticed that there were some reddish, raised tender areas scattered over her body. Eleven days ago the family physician was called and ordered her to bed, thinking she was ill with grippe. Up to this time she had been trying to carry on her school work, although it became an increasingly difficult effort due to the persistent listlessness and loss of ambition. During the eleven days prior to my first seeing her, her temperature ranged between 99° F. in the morning and 101° F. in the afternoon and evening. The past few days she has complained that she "hurts all over" to touch and on being moved. A special inquiry was made as to joint pain or ache and the patient denied having any. During the past five days there has been occasional nausea but no vomiting. Ten days ago she had a slight productive cough that has practically disappeared now. Two days ago and also yesterday there was a moderate epistaxis. During the past few months her weight has averaged between 125 and 130 pounds and for the past two years the patient has tried to diet with a view to keeping her weight down and possibly losing a little. In searching for some infection which may have been present just prior to this present illness the history

elicits nothing except the presence of a slight head cold about two to three weeks ago.

Past History.—Tonsillectomy was done at three years. Prior to this there was no attack of tonsillitis. At eight years of age became ill, complaining chiefly of much fatigue and listlessness and she was ordered to bed by the family physician because the "heart was in poor condition." The mother was told that "the tonsillitis germ went to her daughter's heart." Duration of stay in bed was about two weeks, after which time she seemed well and regained her strength and well-being. At nine years of age her left hip suddenly became stiff. A cast was applied and removed in a few weeks. There was no pain at this time and there has been no recurrence of this trouble since then. From this period until the age of fifteen the patient was well and indulged in athletics at high school, playing basketball and tennis. At the age of fifteen she became ill with nausea and vomiting, being unable to hold any liquids or solids and at this time was in bed for about two weeks. About four or five years ago, while playing tennis, her face became very blue and she nearly collapsed. During the past few years the patient has noticed the sudden appearance of what she describes as "little moles" on the skin. These would disappear after a period of a few days to some weeks. The only form of exercise indulged in during the past few years has been horseback riding and walking, and this has been with the consent of the family physician. In recent years a few dental cavities were filled, but no *x*-ray studies were made of all the teeth.

Menstrual History.—Onset at thirteen years, each cycle being of three to four days' duration. For four years after onset the menses were very regular, and then without apparent cause there was amenorrhea for one year. In the following six months there were two menstrual periods and during the past year there have been five, usually of about three days' duration.

Family History.—There is nothing relevant here and no story of cardiovascular disease.

Physical Examination.—The patient was seen lying in bed, conscious and rational, complaining that her entire body was

tender to the slightest pressure. *Pulse-rate* 108, regular and of good volume and tension. *Temperature* 101° F. *Blood-pressure* 130 systolic, 50 diastolic. *Respirations* 24, and aside from the slight increase in rate were not remarkable. *Head:* There was nothing noteworthy except a few discolored teeth and some that showed dental fillings. The tonsillar fossæ showed no remaining tonsil tissue. The chest was symmetrical; the respiration was not labored. *Heart:* The right border was 1 cm. to the right of the midsternal line and the left border was 12 cm. to the left of this line. There was no increased dulness at the base. The apex was felt in the fifth interspace and there was no thrill. Over the entire precordia there was heard a blowing systolic murmur with the greatest intensity at the apex. The murmur was transmitted to the axilla. The pulmonic second sound was markedly accentuated and of greater intensity than the aortic second. The *lungs* showed nothing remarkable. The *abdomen*, because of the general tenderness, apparently in the skin, could not be satisfactorily examined. *Extremities:* Showed nothing remarkable, aside from the notations of the skin as follows: Scattered over the lower legs, the upper extremities, the abdomen and trunk were some purplish-red elevated areas fading slightly on pressure and definitely tender. These areas were generally from $\frac{1}{4}$ to 1 cm. in diameter, and rather nodular.

Impressions at the First Visit.—It was apparent that the patient had an infection of rather insidious onset, dating back some seven or eight weeks, slowly progressive, causing a moderate febrile reaction and a gradual depletion of strength. The more common diseases giving such a syndrome are typhoid and paratyphoid fevers, tuberculosis, sepsis, and endocarditis. Certain laboratory studies were deemed advisable as soon as they could be done, and in the course of a few days the following results were obtained:

The Widal test for Bacillus typhosus and paratyphoid A and B was negative.

Bacterial examination of a blood-culture[1] was negative.

[1] All blood specimens in this case, for culture, were transferred into beef infusion broth.

The white blood-cell count was 8000.

Urine: Single specimen, acid, specific gravity 1.015, albumin slighest possible trace. Sugar 0. Sediment: Rare red blood-cells, occasional white blood-cells.

Conclusions.—The negative Widal reaction, the absence of a leukopenia, no enlargement of the spleen together with no traceable typhoid history all tended to rule out this disease. Sepsis such as is seen following surgical or obstetric conditions was ruled out by a negative history. The possibility of further investigation with tuberculosis in mind would have to be considered if the patient's signs and symptoms were unaccounted for by some other diagnosis. It seemed, however, that with no findings to substantiate any other condition a diagnosis of endocarditis was the most logical one, being either a lighting up of an old process or a new superimposed infection. To substantiate this is the history of a slowly progressive, insidious infection; a history of "heart trouble" at eight years; a definite endocarditis (mitral regurgitation) found at this examination; and tender nodules scattered over the body which were diagnosed as being erythema nodosum, a condition which is a manifestation of an infection with the "rheumatic streptococcus," just as is chorea, or rheumatic fever, and is strong evidence in support of a conviction that one is dealing with a streptococcus infection of a type that often involves the endocardium. The purpose now was to keep repeating blood-cultures with a view to isolating the infecting organism, thus to definitely establish the diagnosis of bacterial endocarditis. It must be borne in mind that in this condition the organisms may not be in the blood-stream constantly, only being intermittently thrown off from the heart valves or walls, and for this reason we frequently obtain negative cultures. It is also probably true that the blood-stream may disinfect itself in about forty-eight hours if there is no focus delivering organisms to it, so that we must do bacterial examinations of blood-cultures frequently, and in cases showing a repeatedly negative result we may influence the result by obtaining the blood-culture at a time of day when the temperature is highest.

In pondering over the history of this patient's present illness one is led to feel that given a patient with a temperature that is continued over a period of a few weeks, some explanation other than grippe—a condition that should subside within a week—should be sought. Influenza, uncomplicated, may go on for ten days to two weeks, and if at the end of approximately this time we find no change, it is reasonable to suppose that the continued fever is due to some disease that runs a subacute to chronic course rather than an acute one. The most common of these have been mentioned above. Further analysis of the present illness shows that for about six weeks prior to calling the family physician the patient had been having symptoms that were definitely important, especially when we consider that this patient had a past history of heart trouble. The mother of this girl prided herself on the care and thought she gave her daughter, and yet she did nothing for many weeks. This is probably explained by two factors: first, that the patient was not of the complaining type and, second, that the mother had not been instructed properly as to how serious any seemingly unimportant infection may be to a person with a past history such as we have here. During the two years previous to the present illness the patient had been seen periodically by some physician who, according to the mother, always made light of the patient's heart condition, telling her that everything would go on all right and to do nothing but restrict exercise to horseback riding and walking. The tennis and basketball that this girl indulged in were surely ill-advised and it seems that any exercise should have been carefully graded and the effect on the patient watched closely. In this case neither the patient nor the family were ever given any real insight into the problems to be faced when endocarditis is present. Individuals with rheumatic heart disease should themselves be told, if it seems feasible, or if not some responsible party, that any progressive trend of symptoms, such as we have had in this case, or any infectious disease, no matter how trivial it seems, calls for medical observation very early. Another point of interest is that there is a history of the patient trying to lose weight during the few years prior to this illness.

Just how important this fact may be is problematical, but it does seem that persons with organic heart disease are better off with probably 10 pounds or so more than their normal average, especially until they reach the fourth decade of life, when the incidence of bacterial endocarditis drops off markedly. As a general principal, if these cases are not too much overweight they should not be allowed to diet with a view to reducing, for by doing so they may lower their resistance and well-being, making them more prone to intercurrent infection.

From the history it seems reasonable to suppose that the present infection became active in early January. Whether or not putting the patient at total rest at this time would have made any difference in the progress of her illness, no one can state. However, from this time until late February, when she was ordered to bed, much precious energy was being used up. This undoubtedly further lowered her vitality and resistance, and as it is extremely important in treating bacterial endocarditis that the individual's resistance be maintained at its maximum level, it seems that bed rest is one of the things that should be instituted as early as possible.

Prognosis.—The family was given a poor prognosis, being told of the extreme seriousness of the disease and that, if we eventually were able to demonstrate a streptococcus in the blood-stream it would conclusively prove the diagnosis and mean that we were dealing with a disease from which recovery was only very rarely reported. The patient, a very intelligent, sensible and co-operative girl, was told that she had a rheumatic infection—no mention being made of the heart—and that she would be in bed some months. This was accepted by her quite philosophically and so far as one could judge did not upset her mental peace to any extent.

Early Treatment and Course.—Absolute rest in bed was ordered and it was possible to institute constant nursing attention. Two days after first seeing the patient she was started on sodium salicylate effervescent, 40 grains, daily. Three days after this the tender nodes stopped aching and the only complaint was night sweating. The blood-pressure was 125 systolic

and 45 diastolic; there was a pistol shot heard in both groins; with the lowered diastolic pressure and the pistol-shot sounds in the groins, the question of an aortic regurgitation came up, but there was no diastolic murmur over the aortic area, no capillary pulsations, and no pistol-shot sounds at the elbow. At this time the liver was not enlarged or tender and the spleen was not palpable.

White blood-cells 12,000, red blood-cells 3,800,000, hemoglobin (Talqvist) 70 per cent.

Smears.—Polymorphonuclear leukocytes 65 per cent., lymphocytes 30 per cent., mast-cells 1 per cent., endothelial cells 3 per cent., eosinophils 1 per cent.

The red cells, aside from showing a moderate degree of achromia, were not remarkable. A mild secondary anemia was present for which soft mass Blaud pills, 15 grains, daily, were given. The diet was not restricted.

x-Ray films of the teeth, taken March 17th, showed one abscessed root and two that were very suspicious. To eliminate every possible focus of infection all of these teeth were extracted by March 25th. The films were taken and the extractions done without the patient leaving her bed, and caused no untoward reaction whatsoever.

The sodium salicylate (dosage as above) was continued for four weeks and then the amount was raised to 80 grains a day for ten days. This large dosage in no way disturbed the gastrointestinal tract. During the first few days of treatment with this drug the erythema nodosum completely subsided and at no time returned. During the five and a half weeks of treatment with the salicylate there was no definite change in the pulse-rate, which was generally between 100 and 110 beats per minute. The temperature during the first four weeks of salicylate therapy suggests a slow, irregular dropping to normal by lysis; however, the day following this (April 8th) the temperature again rose to 101° F. During the next week another drop to 99° F. (by lysis) occurred and then the temperature became the "picket-fence" type. About this time the salicylate was stopped, as it seemed to have no definite effect on the course of the disease.

On April 6th it was decided to start sodium cacodylate and the patient was given $3\frac{1}{2}$ grains subcutaneously once a day.

A blood-culture taken April 12th proved to be positive, the organism being a non-hemolytic streptococcus which grew with difficulty and showed morphologically considerable pleomorphism, and it seemed to grow better anaërobically than aërobically. Small[1] and Birkhaug[2] both described this type of organism as the cause of rheumatic fever. It is the "gamma" streptococcus from the classification by Smith and Brown[3] and it will be recalled that they classified streptococci as alpha (viridans), beta (hemolytic), and gamma (non-hemolytic). Five days later, on April 17th, the blood was again cultured and the same organism was found. It seemed now that our diagnosis was definitely established.

The general condition of the patient was steadily improving; she slept well; her appetite was fairly good; her strength seemed to be increased; her mental state was excellent; and the atmosphere of the sick room was all that could be desired, in that the family and nurses kept the patient cheerful and optimistic at all times.

April 30th the white blood-cells were 11,000; red blood-cells 4,500,000; hemoglobin (T.) 70 per cent.

The temperature during the preceding two weeks was of the "picket-fence" type with an occasional day when it was normal at 8.00 A. M. and 4.00 P. M. The four-hour chart on these "normal" days showed about 1 to 2 degrees rise in the late afternoon and evening. The morning temperature was usually normal or subnormal; while in the afternoon it was not over 100.6° F. as a rule. The night sweating had stopped about two weeks previously and to further the feeling that there was some gain being made in the general condition there was a rise in the red blood-cells and an absence of any subjective signs of toxicity. The patient did not seem to be losing any appreciable amount of

[1] Small: Amer. Jour. Med. Sci., 1927, vol. 173, p. 101.

[2] Birkhaug: Jour. of Infect. Dis., 1927, vol. 40, p. 549.

[3] Smith and Brown: Monograph Rockefeller Institute No. 9, January 1919.

weight. To date she was withstanding the infection very well. However, it should be stated that at no time was the original prognosis changed and the fact that recovery was practically impossible was not forgotten, in spite of the various clinical evidences of improvement.

The sodium cacodylate was used daily since April 6th, and as there were no untoward effects, the dosage was raised to 7 grains, once daily, on May 1st. This treatment was maintained steadily until May 23d, on which day it was omitted because of an anaphylactic reaction which will be taken up under "complications."

Complications, Further Treatment, and Course.—On April 25th the patient complained of tenderness at the end of the left ring finger and on examination it was noted that the extreme end of the ventral surface of the distal phalanx was purplish red and tender to pressure. The area was no larger than a pea and it came on rather suddenly, being called to the patient's attention by the tenderness; both this and the discoloration were gone in three days. Undoubtedly an extremely small (probably microscopic) embolus lodged in this area causing an infarction. This was the first known embolus in this case and gave further assurance of the correctness of the diagnosis. As the case progressed emboli became more and more numerous and frequent, and they probably originated from the vegetations on the mitral valve.

During the afternoon of May 6th there was a sudden sharp pain in the left upper quadrant, and the temperature rose to about 101.5° F. which was definitely higher than any afternoon temperature during the preceding week. Within a few hours changing of position and deep respiration or yawning caused sharp pain in this same area. On examination the area was very tender and spastic. There was no evidence of any pleural or diaphragmatic condition causing the above symptoms. The following morning the edge of the spleen was palpated without difficulty, the spasm continued, and the patient complained of much tenderness during the examination. The white blood-cells rose to 20,000 and the temperature dropped to 99.2° F. The pain on motion,

deep respiration, and yawning grew worse and there also developed a gastro-intestinal upset manifested by distension, loss of appetite, and nausea. On examination no evidence was found of pleural or diaphragmatic involvement and a diagnosis was made of splenic embolus with infarction. The above symptoms gradually subsided and on the sixth day there was no complaint relating to the splenic infarction. The spleen, however, remained palpable at this time although it seemed smaller. During this period the cacodylate was not discontinued and with the subsidence of the symptoms there was a return of the well-being which the patient had experienced prior to the splenic embolus. I wish particularly to call attention to an interesting development directly following the splenic infarction and undoubtedly related to it. It will be recalled that with the embolus the temperature rose sharply. On the third day following this it became normal having dropped by a rather rapid lysis, and by consulting the temperature charts it will be observed that for approximately seven and one-half weeks after this, barring some rises that will be explained by further complications, the temperature changed in character from a "picket-fence" type to one that was normal for many days at a time, and when there was an increase it was very slight. It seems reasonable to explain this as follows: An embolus carrying organisms with it lodged in the spleen, causing an infarction and an acute inflammatory reaction; this, in fact, was an auto-vaccination resulting in a definite leukocytosis and the production of antibodies, and because of the beneficial effect this seemed to produce it was decided to make and administer an autogenous vaccine. This phase of the treatment will be taken up later.

The drop in temperature following the splenic infarction maintained itself for about nine days when it was noted that the afternoon temperature was slightly increased (99° to 99.4° F.) and then, on May 23d, during the afternoon the temperature suddenly rose to 103° F., and the pulse-rate to 120. Definite urticarial wheels appeared scattered over the face, neck, trunk, and extremities, the patient was flushed and complained of nausea, epigastric distress, and itching. As no dietary changes

had been made, and as there was nothing new in the patient's environment, it seemed that the causative factor of this anaphylactic reaction was the sodium cacodylate which had been administered daily since May 1st, in 7-grain doses. The drug was discontinued with the appearance of the urticaria and the subcutaneous use of adrenalin chlorid, in 5-minim doses of a 1 : 1000 solution, controlled it. It was necessary to give three doses within forty-eight hours and at the end of this time the temperature had dropped to normal, all anaphylactic manifestations had disappeared and for nine days the temperature continued essentially normal. During this period the patient had a return of the well-being experienced previous to the onset of the urticaria, she had absolutely no complaint, sat up in bed often, was happy and cheerful and stated that she was feeling better than at any time during the few months preceding her present illness. The heart findings remained as noted previously and the spleen at this time was no longer palpable.

On June 3d during the afternoon the patient experienced a rather severe aching in the right loin which became somewhat more exaggerated during the night. The temperature rose to 100° F. and the pulse-rate went up about ten beats per minute. The following morning the white blood-cells were 32,000, the red blood-cells 4,000,800, and the hemoglobin (T.) 65 per cent. The urine showed an increased amount of albumin, more white blood-cells in the sediment, and a few red blood-cells were also seen. The patient complained of some nausea, loss of appetite, and on deep breathing increased pain in the right loin and right umbilical region. A diagnosis of right renal embolus with infarction was made. Here again we probably had another autovaccination with a resulting leukocytosis and antibody production, following which the temperature continued normal and the pulse-rate dropped to between 80 and 90 from a former average between 90 and 100.

On June 8th the white blood-cells were 17,600, the pain in the right loin had entirely disappeared, and there was a return of the patient's well-being. During the following three weeks the temperature was essentially normal with the exception of two

consecutive days, when it rose to about 99.5° F. in the afternoon. This rise could not be explained by any complication and the patient had no complaint. At this time the white blood-cells were 13,200, the red blood-cells 4,500,000 and the hemoglobin (T.) 75 per cent. The period from May 8th, immediately following the splenic infarct, until June 30th, approximately seven and one-half weeks, was one during which from a clinical standpoint the patient was doing well, and it seemed reasonable to suppose that the greatest amount of beneficial effect resulted from the auto-vaccination, in both the spleen and kidney, by septic emboli. One cannot estimate the part that sodium cacodylate played in bringing about the apparent improvement and all that can be said is that it was administered continually for about four weeks previous to, and about two and one-half weeks following the splenic infarct, when it was discontinued because of the urticaria.

In addition to the increased well-being of the patient and the improved temperature curve the pulse-rate also indicated that the infection was less active than before the splenic infarct. Previous to this time it ranged between 100 and 110; following this for about three and a half weeks it stayed between 90 and 100 until the renal infarction, when there was a slight rise with the elevated temperature, and then it dropped to between 80 and 90. Surely during this period of seven and a half weeks, with the patient feeling as though she could get out of bed and saying that she felt fine, and with the clinical chart giving added evidence of improvement, there was some reason to feel that possibly this was one of the rare cases that would go on to recovery. This patient had been ill for over four months and instead of steadily losing ground, as is usual in most cases of bacterial endocarditis, she was progressing as well as could be desired and during the past seven and one-half weeks there was unquestionably improvement in her condition and every indication that the infection was less active. These facts tended to insert a bit of optimism into the prognosis and yet, in spite of the above picture, one could not lose sight of the fact that the disease practically always proved fatal, even though there is one or more

periods of remission, and also that there always lurked the danger of an embolus doing permanent harm or causing sudden death.

During the first week of June another blood-culture was taken, the organism previously described (a non-hemolytic streptococcus) was cultivated and made into an autogenous vaccine. An initial dose of ten million organisms was given intradermally to determine if there was any sensitiveness, and as this failed to produce any reaction whatsoever treatment was started on June 9th with a dose of fifty million, which caused neither local nor constitutional reaction. The vaccine was given every five to seven days, depending on the degree of local reaction, a condition which did not occur until the dose reached 150 million, when a small red area the size of a dime was produced and disappeared in about three days. This treatment was continued approximately seven weeks at which time the dose had reached 400 million, the patient having received a total of 1800 million organisms during this period. Vaccine therapy was started a few days following the renal infarct, which was during the time when the patient seemed to be gaining ground. During the first three weeks of this treatment, with the exception of two days, the temperature remained essentially normal until about July 1st, when it began to run an irregularly elevated course, the pulse-rate rose from between 80 and 90 to 90 and 100, and the white blood-cells were 10,600. This condition prevailed without any apparent change in the patient for about two weeks when the temperature again became normal, remained essentially so for six days, and then started another irregularly elevated course which gradually became worse during the following five and one-half months when my active observation of the patient ceased for reasons which will be explained later.

At the time of discontinuing the vaccine treatment it was felt that nothing beneficial had resulted from it. It will be recalled that this treatment was started during a time considered very favorable in that the patient was doing well clinically, had been auto-vaccinated twice, and had experienced a drop in pulse-rate and temperature. Nevertheless, while the vaccine was

being used, this favorable picture changed to one showing an elevated temperature and an increase in the pulse-rate.

The renal and splenic "vaccinations" very probably caused the improvement noted, and yet augmenting this with an autogenous vaccine was of no apparent benefit. It is probably true that the potency of the auto-vaccinations very greatly exceeded that of the autogenous vaccine, as the former were followed by an inflammatory reaction at the site of inoculation, a definite leukocytosis, a moderate rise in temperature and discomfort to the patient, while the latter at no time caused any constitutional reaction, and only a mild local reaction which disappeared in a few days. With these facts in mind it seems probable that too much conservatism was displayed in using the autogenous vaccine and it is reasonable to assume that if any beneficial results are to be obtained from such treatment they will not be brought about until such time as we determine to give repeated massive doses of the vaccine, sufficient to produce definite local and constitutional reactions such as were seen following the splenic embolus. The use of vaccines is based on the theory that intoxicated tissues do not activate antibody formation as well as healthy tissue, therefore by administering vaccines subcutaneously, into healthy areas, we hope to set up new mechanisms for their production. In cases such as this one, and also in other forms of septicemia, it seems that there is nothing to lose by making highly concentrated vaccines and giving them in very much larger doses than is the routine at present, an idea that was used in giving the patient "immunized transfusions," which will be described later.

After discontinuing the vaccine it was decided to give the patient some scarlet fever streptococcus serum, and accordingly on July 30th she received one dose of 30 c.c. intramuscularly, the gluteals being the site used. The infecting organism being a streptococcus it was thought that a streptococcic serum might in some way produce a favorable action, or possibly an increased leukocyte count with a rise in temperature, but no constitutional reaction was noted and locally there was nothing more than a slight soreness for a few days. A few hours before the serum was

administered the white blood-cells were 24,600, the red blood-cells were 4,280,000, and the hemoglobin (T.) 60 per cent., while the following day the white blood-cells were 23,800, and it was felt that giving the serum was rather a futile gesture. At this time the physical examination was unchanged, excepting for some hypertrophy of the left ventricle which was 13 cm. from the midsternal line. The patient continued to feel well and to be very cheerful. The following three weeks the temperature became more and more "picket-fence" in character with a gradually increasing afternoon rise, and during this period there were many minute emboli causing small infarctions at the ends of two toes, one finger, and in the skin of the neck and trunk. The patient's attention was drawn to these by soreness that developed suddenly and on examination purplish-red areas, the size of a pea or even smaller when in the skin, were seen. These disappeared in from three to five days. The above occurrences undoubtedly indicated that the infection was becoming more active and with the increasing embolic manifestations it was not surprising that during the early morning of August 20th there occurred a cerebral embolus. The nurse reported that she was awakened by a shrill cry from the patient, who immediately seemed to stiffen from head to foot and then lapsed into unconsciousness. When she was seen, within a half hour, she could not be aroused, her pulse had dropped to 60, the blood-pressure was 90 systolic and 65 diastolic, and the skin was cold and clammy. Further examination was not done at this time, as it seemed best not to disturb the patient, but the following day a superficial neurologic examination revealed a right hemiplegia and a right facial paralysis. The unconscious state persisted for seven days and during the fourth and fifth days the pulse was very feeble and at times irregular, the skin extremely cold and moist, the heart action very weak, and it seemed that the patient would not survive, and yet at the end of a week she began to regain consciousness, the pulse volume and rate improved, the systolic blood-pressure rose to about 110, and the skin became less clammy and warmer. No drugs were given during this period and the treatment consisted of general nursing care and rectal feedings of 6 ounces of

milk with the white of an egg every six hours, all of which were retained. On the eighth day full consciousness had returned and it was found that in addition to the right facial paralysis and right hemiplegia there was an aphasia which was nearly complete as the patient could say only "yes." About ten days after the cerebral embolus occurred the facial paralysis began to improve and in about a month was practically gone. However, during this time the condition of the patient was growing worse, the left heart border was nearer the axillary line ($13\frac{1}{2}$ to 14 cm. from the midsternal line), there was evidence of loss of weight, the temperature was elevated from 1 to 3 degrees in the afternoon, the pulse-rate was between 110 and 130, the respirations became more rapid, the appetite was poor, only liquids and semisolids being taken in very small amounts, there was a gradual loss of strength, an anemic appearance was developing, and although a few more words could be spoken, there was no evidence whatsoever that the hemiplegia was improving. It was apparent also that during the past month the blood carried great numbers of very small emboli as there frequently occurred small areas of infarction, either at the end of a toe or finger or in the skin of the neck, trunk, and extremities, and when these latter occurred there was usually from one or two to probably eight or ten scattered areas of infarction, acting similarly to those previously described. The rectal feedings were continued, as very little food was taken by mouth, often there was nausea and vomiting following any form of nourishment, and at times without any relation to food or drink.

During the week preceding and the four weeks following the cerebral embolus the infection became more active, and as the patient was gradually growing worse clinically it was decided to give a series of transfusions, using donors who previously were given a course of vaccine made from the patient's organisms, so-called "immunized transfusions." The family was told that this form of treatment had been unsuccessful in the past, and that no cure could be expected following its use here. However, feeling that they wished nothing left undone, universal donors were obtained and four transfusions were given the patient, using

the following routine: It was explained to the young men used as donors that they were to be given a vaccine made from the patient's organisms and that they should expect a marked local and possibly some constitutional reaction, but that, as far as one could foretell, the procedure would in no other way injure them; in preparing for each transfusion, a new, very highly concentrated vaccine was prepared from recent cultures, and the donor was inoculated with large daily doses, unless a very severe reaction made necessary the lapse of a day or two, the purpose being to give the total amount deemed necessary in about seven to ten days; between the last dose of vaccine and the transfusion, there was an interval of three to eight days, to allow the effect of the vaccine to take place. The Kimpton method of transfusion was employed as it seemed best not to use chemically treated blood; immediately preceding the first three transfusions a blood-culture was taken which in every instance proved positive for the organism previously described, and a known quantity of blood (1 and 2 c.c.) was put into a known amount of citrated broth (2 c.c.) for transferring to agar plates (which was done within thirty minutes) for the purpose of estimating the number of organisms in the blood-stream; these latter two procedures were repeated at varying intervals after each transfusion, the cultures always being positive, hoping that in this way, in addition to clinical observation, either an early or late effect of the transfusions might be estimated; even though universal donors were used, the blood-serum of each one was tested against the recipient's cells to definitely ascertain that no agglutination took place.

O. W. R., the first donor, received within eight days a total of 9950 million streptococci, divided as follows:

September	12, 1928—	300	million	streptococci
"	13, " —	750	"	"
"	14, " —1	100	"	"
"	15, " —1	800	"	"
"	18, " —3	000	"	"
"	19, " —3	000	"	"

He was able to continue his college work, showing locally a reaction about $2\frac{1}{2}$ inches in diameter and constitutionally nothing

more than a very mild malaise with the last three doses. The interval following the fourth dose was because of a rather marked local reaction.

The first transfusion was done on September 26th and just prior to it there were 42 organisms per cubic centimeter of blood, while twenty-four hours later the count was 40 organisms, and five days later (October 2d) it was 27 organisms.

G. B. G., the second donor, received within eight days a total of 12,750 million streptococci, divided as follows:

October	19, 1928—	250	million	streptococci
"	22, " —	500	"	"
"	23, " —1000		"	"
"	24, " —2000		"	"
"	25, " —4000		"	"
"	27, " —5000		"	"

He was able to continue his college work, had a local reaction starting with the fourth dose, similar to the first donor, and the only constitutional reaction was a very mild malaise during the last three days.

The second transfusion was done on November 5th and just prior to it there were 95 organisms per cubic centimeter of blood, while twenty-four hours later there were 35 organisms.

O. W. R., the first donor, was again used for the third transfusion and received within five days a total of 6200 million streptococci divided as follows:

November	16, 1928—	200	million	streptococci
"	17, " —	400	"	"
"	18, " —	800	"	"
"	19, " —1600		"	"
"	20, " —3200		"	"

It was felt that as this man had been inoculated with the same organism about two months previously he could be worked up more quickly, and that the total amount need not be as great as formerly. He continued at his studies and experienced about the same reaction as during his first series of inoculations.

The third transfusion was done on November 23d, and just preceding it there were 65 organisms per cubic centimeter of blood, while three days later the count was 46 organisms.

A. U. D., the donor for the fourth transfusion, received within nine days a total of 17,600 million streptococci divided as follows:

November	24,	1928—	200	million	streptococci
"	25,	" —	600	"	"
"	26,	" —1	600	"	"
"	28,	" —	200	"	"
"	29,	" —2	000	"	"
"	30,	" —3	000	"	"
December	1,	" —5	000	"	"
"	2,	" —5	000	"	"

This man was able to continue his studies until the last two doses, which produced a local reaction about 4 inches in diameter and moderate malaise, necessitating rest in bed for two days. After the third dose it will be noted that there was a lapse of a day before the next inoculation, which was a much smaller amount. The interval of a day was taken because of a marked local reaction, and as inoculations were resumed with a new vaccine prepared from a recent culture it seemed advisable to give a low initial dose. The first six doses caused mild to moderate local reactions and no malaise occurred until the third dose.

The fourth transfusion was done on December 5th, and three days following it there were 46 organisms per cubic centimeter of blood.

In studying the effect of the transfusions on the number of organisms in the blood-stream it is seen that twenty-four hours following the first one there was practically no change, but that five days later the count had dropped from 40 to 27, and while this was a desirable finding, it may well have been nothing more than a fluctuation in no way related to the transfusion. The next count, made just preceding the second transfusion on November 5th, was 95, much higher than the former ones, and seemed to indicate that there was no late effect following the original transfusion. The count made twenty-four hours after the second transfusion had dropped to 35, and in no way was analogous to the situation seen twenty-four hours after the first one, when no change was noted. The next count, on November 23d, just prior to the third transfusion was 65, and here we again see a higher count some weeks following the previous trans-

fusion. No count was made until three days after the third transfusion, when it was found to be 46, a drop that was too small to be in any way significant. No count was made preceding the last transfusion on December 5th, but three days following this it was 46, the same as that done twelve days previously. In estimating the above results one cannot feel that the transfusions in any way diminished the activity of the infection or the number of organisms in the blood-stream, for without doubt such fluctuations as are noted may very well have occurred irrespective of anything that was done. Another futile gesture had been made.

In studying the clinical course of the patient during the period when the transfusions were being given, and also following this time, one comes to the same conclusion as regards the infection that is noted above, and, in fact, one must go a step further and recognize that the picture was progressively growing worse in every way. The temperature was definitely of a "septic" character, being normal or only very slightly elevated in the morning and rising to between 100° and 102.5° F. in the afternoon, the pulse-rate was between 120 and 130 and the respirations rose to between 35 and 40 in the afternoon, both being somewhat lower during the morning. On October 2d there was evidence of another splenic embolus with the same symptoms as during the first one. The spleen was enlarged and tender and the pain in the left upper quadrant lasted for about six days and was aggravated by motion, deep respirations, and coughing. During this time the appetite was poor, there was intermittent nausea and vomiting, unrelated to meals, and the abdomen was distended. As the weeks progressed the strength of the patient gradually decreased, she complained of being tired all the time, her interest in the surroundings grew less, there was a very noticeable emaciation taking place, the skin was becoming very sallow and very often there were showers of petechial hemorrhages scattered over the face, neck, trunk, or extremities. At other times showers of emboli would strike an extremity or an area of skin often 5 or 6 inches in diameter, causing infarctions which were usually small and disappeared within five or six days.

Countless numbers of these hemorrhages and infarctions were occurring, giving further evidence that the infection was progressively growing worse and was constantly throwing organisms into the blood-stream. There was no evidence whatsoever of any improvement in the hemiplegia or the aphasia and the entire right side of the body was defintely atrophied. Following the cerebral embolus the patient could not take other than liquid and semisolid foods in amounts usually not over 6 or 7 ounces, and as time went on the semisolids taken grew less and less, and the amount of liquid taken at any one time was usually less than 3 or 4 ounces. Rectal feedings were resorted to and fortunately were retained after constant use during periods of two to four weeks.

About the middle of October the patient began to complain of substernal heaviness and fullness; the left heart border was at the anterior axillary line, the spleen remained palpable but not tender, there was frequent abdominal distention with a vague pain in the lower abdomen at times, and there occurred intermittent periods of sweating, especially during the night. There was an increasing loss of appetite, it being necessary to coax the patient to take even a few ounces of liquid. The days without nausea and vomiting were becoming fewer and farther apart, the weakness grew greater and a desire to sleep was nearly always present. As our story goes into November, we find the patient having a few severe crying spells with much depression, an increasing inability to take even liquid nourishment without nausea and vomiting, and complaining of pain in the left hip, the cause of which could not be determined, as on examination nothing was found to account for it.

On November 11th a very minute embolus lodging in the brain manifested itself by a sudden cry, immediate unconsciousness, and a general convulsive spasm of the entire body, during which it was impossible to open the patient's mouth. Consciousness began to return in about ten minutes and it seemed that the action of the mouth, tongue, and throat was impaired. In about thirty minutes, however, the entire episode had subsided and the patient's condition seemed unchanged. Throughout most of

November the temperature, pulse, and respiratory curves were somewhat lower than during the preceding month and as this occurred during a period following the first two transfusions some possible relationship between them suggests itself. However, the temperature chart in this instance belies the clinical picture, which was growing steadily worse and the apparent improvement that the chart indicated was probably due to progressive lowering of the vitality and resistance and increasing emaciation. The pulse-rate, while somewhat slower, was becoming smaller in volume and irregular at times and the respirations were very shallow, especially during sleep. Muscular twitchings about the mouth were becoming frequent, the amount of liquids taken was growing less and on both November 16th and 29th there was evidence of a new splenic infarction, with complaints and symptoms as during the first one described.

The nausea and vomiting grew worse, the former often continuing most of the day and the latter occurring as often as four and five times. In an endeavor to control these conditions the following drugs were tried individually: Cocain, anesthesin, tincture of nux vomica, compound tincture of gentian, chloroform water, cerium oxalate, and tincture of opium; there was no benefit derived from any of the foregoing. An unusual feature was that it was possible to give rectal feedings of peptonized milk and egg every six hours for many weeks at a time without the occurrence of irritation and the expulsion of part or all of the nourishment. There was much restlessness during the night and day and this could be controlled by either allonal or morphia.

The last transfusion was given the morning of December 5th, and during the afternoon the patient complained of soreness along the anterior aspect of the left thigh. The following day there was considerable pain from the left knee up into the left groin on any motion, and two days later there was a definite area of swelling, 3 inches in diameter, about the femoral artery just below the left groin. There was no redness. Palpation revealed tenderness and a marked thrill, and on auscultation there was a rough, loud, blowing murmur synchronous with cardiac systole, all indicative, it seemed, of an arterial thrombosis. During the

next two weeks the tenderness and swelling gradually diminished and the thrill disappeared, the murmur, however, remained loud and blowing in character.

On December 18th another cerebral embolus occurred causing a lapse of consciousness and a convulsion, both of which lasted about ten minutes. The patient's condition grew worse constantly during December, the weakness increased steadily, the color grew more sallow, the pulse was rapid, often irregular and of poor quality, respirations were rapid and shallow, vertigo with a blurring of vision occurred frequently, emboli in great numbers were constantly manifesting themselves in the skin of the face, neck, trunk, and extremities, and also the soft palate, the lower jaw seemed too weak to hold a thermometer in place and the muscles of mastication seemed unable to function for over a few miments at a time. The skin was dry and very warm, emaciation was extreme, and severe epistaxis occurred a few times. The breath was very foul, there was considerable itching of the skin generally and, on December 23d, there occurred a fifteen-minute period of general body twitching, jerky movements of the extremities and rolling of the eyes, a picture which recurred several times that day and the next. The patient dozed almost constantly during these two days, the pulse was poor and irregular, the respirations very shallow and it seemed that she could not survive many more days. No menstrual flow had occurred since July. Throughout the entire course of the disease there was no evidence of pulmonary complications or of gangrene, even though emboli were frequent and numerous.

The family was informed of the situation and insomuch as they were told that there was nothing further to try medically, they supplanted physicians and medical care with "Christian Science." Accordingly, on December 24th, two "Science" nurses and a practitioner assumed control of the patient. After this the author visited the patient three or four times but merely as a friend, and it was during one of these calls that he was discovered counting the pulse-rate, whereupon it was suggested that he never do so again as "Science" does not allow it. A request was then made, in a very friendly manner, that he omit

all calls to the house until the patient was cured, as his thoughts, being a physician, were not proper and undoubtedly interfered with the healing of the patient. For many months preceding the change to "Science" the immediate family had been studying it constantly, and a practitioner had been giving "absent treatment" to the patient, so that it was a natural sequence that they gave themselves over to it entirely, especially after the case had been given up as hopeless. The change was made in an amiable manner, without opposition on the part of the doctors in attendance, and the author has had friendly telephone communication with the family on several occasions. All that could be learned concerning the patient in this manner, was that she "is doing very well," that thanks are given for what each day offers and that they do not look into the future more than one day at a time. From the maid in the household, it is learned, however, that the patient looks worse than ever, says even less than the few words she used to utter, appears to sleep most of the time, and takes very little in the way of food or fluid.

The last word heard relative to the condition of the patient was contained in a short note dated January 21, 1929 received from a sister, which said "everything is going along nicely." It is evident of course that the ultimate result of this case cannot be noted at this time, but one may rightly say, it seems that it is quite inconceivable to foresee any outcome except a fatal one.[1]

In the introduction mention was made of cases of subacute bacterial endocarditis reported as recovered, undoubtedly a spontaneous occurrence, and this possibility, even though extremely remote, was present in this case.

As one thinks back and pictures this disease and its complications, there comes a realization of the tremendous problems that must be met in trying to find an adequate therapy.

It seems that in the early stages, before complications occur, the problem is not entirely one of blood-stream sterilization, but one involving the obliteration of the foci of infection on the heart

[1] This patient died in a markedly emaciated condition on February 28, 1929.

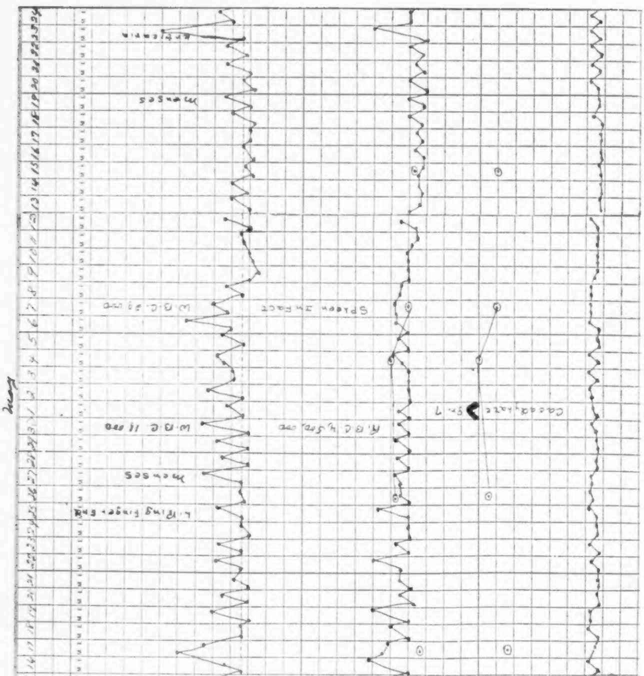

Fig. 33.

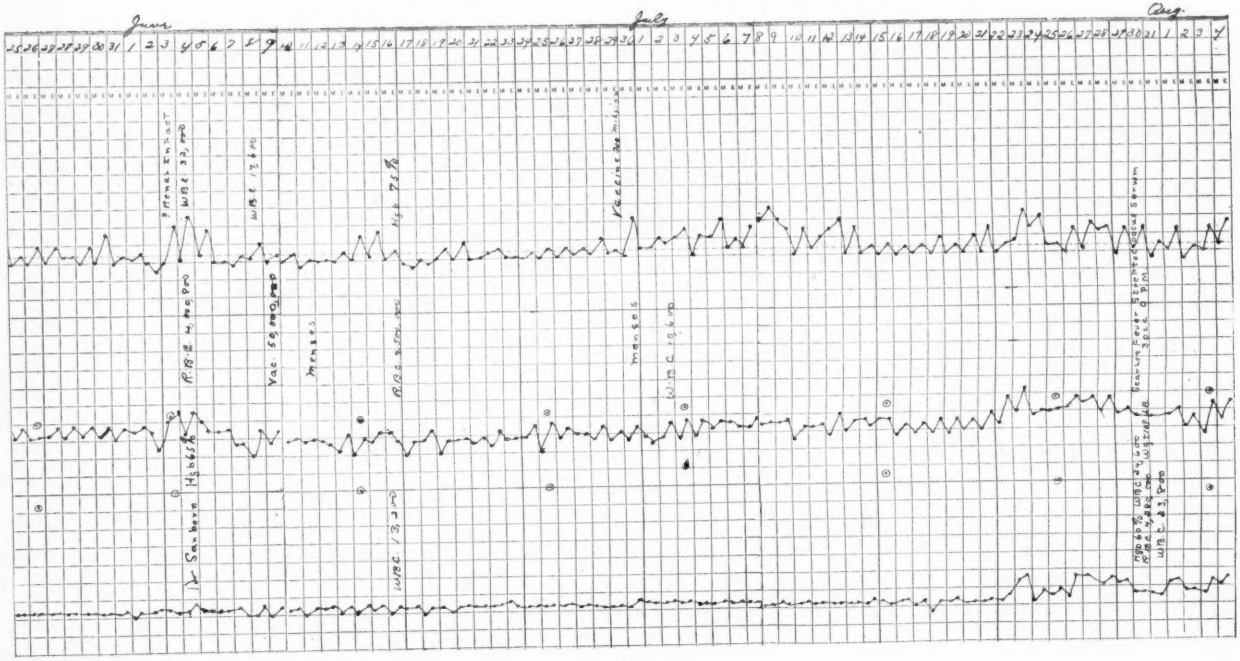

Fig. 33.—Continued.

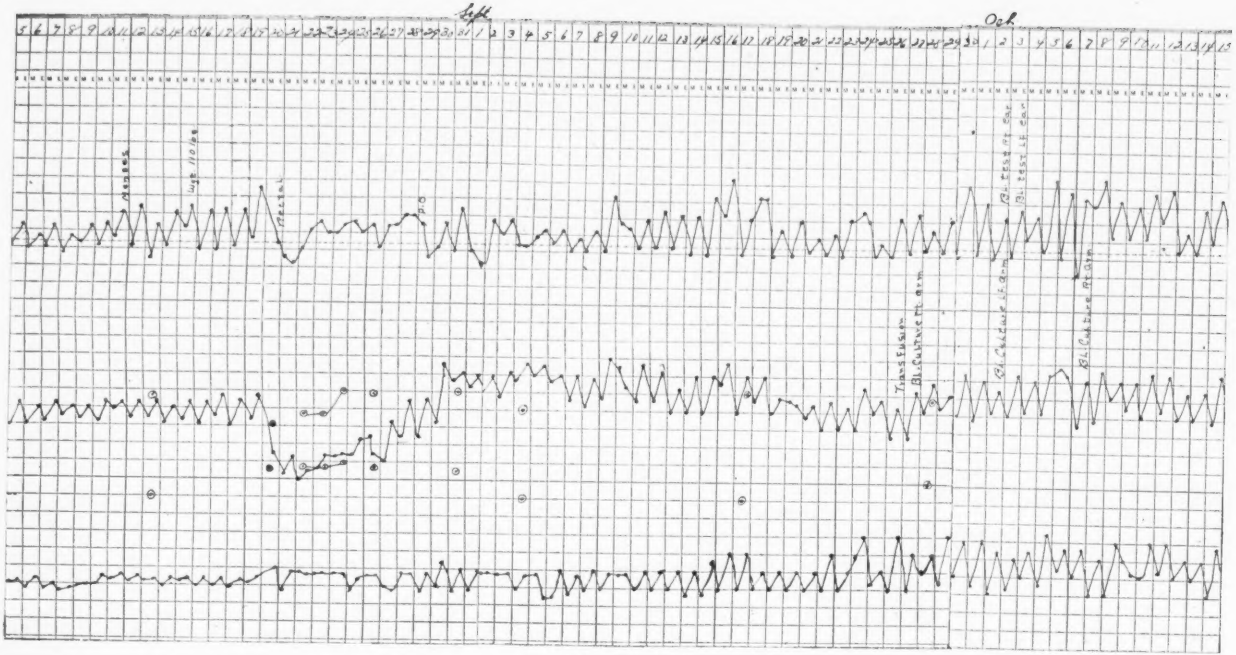

Fig. 33.—Continued.

Fig. 33.—Continued.

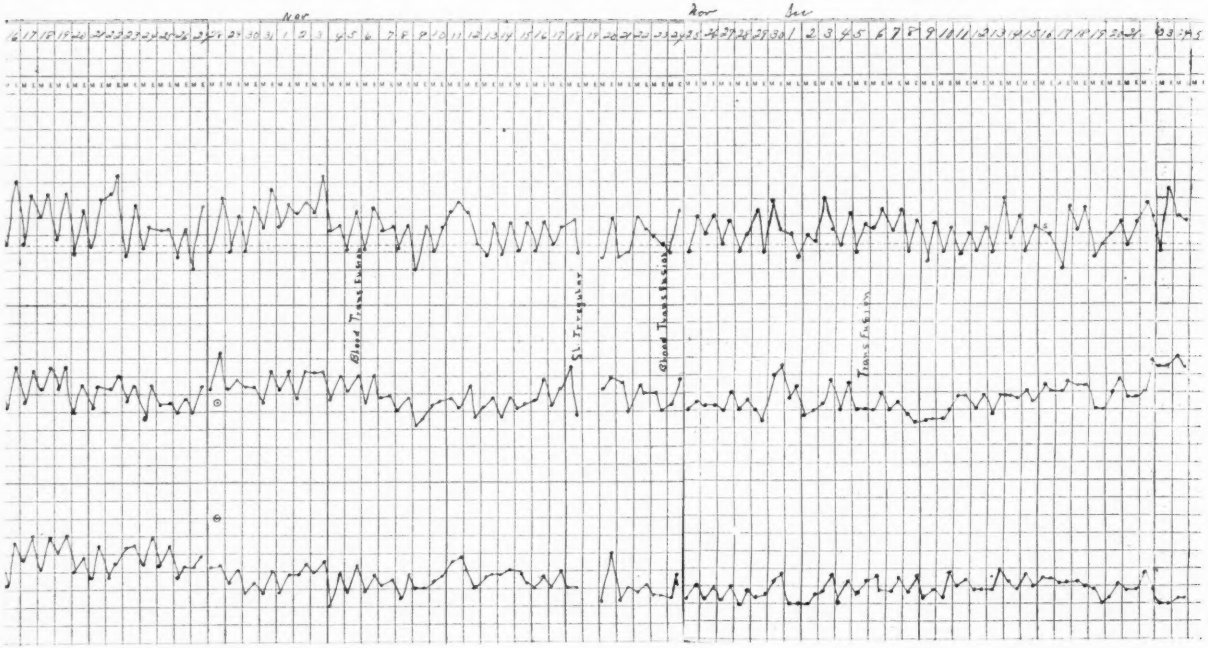

Fig. 33.—Concluded.

valves, for no matter how often the blood-stream is sterilized, if the foci are not obliterated, organisms will again be given off into it.

It is also quite certain that the heart does not alone contain foci for wherever emboli lodge, and especially if they are followed by inflammatory reactions, it is probable that they have carried organisms with them, creating new foci, any of which, even though they lie dormant for lengthy periods, may flare up at any future time. With these facts before us it becomes apparent that any chemical agent used to combat the infection must, in addition to sterilizing the blood-stream, reach the infecting organisms whether they are in the valvular vegetations or in other organs. As was mentioned previously, it is quite probable that if all foci were obliterated, the blood-stream might become spontaneously sterilized.

However, even though we might conquer the infection, obliterate all foci and bring back our patient's health, there will ever remain the dreaded possibility of future emboli resulting in paralyses, infarctions, gangrene, or death.

RECORD OF URINALYSIS

Date.	S. G.	Reaction.	Albumin.	Sugar.	Diacetic.	Sediment.
3/29/28	1014	ac	Tr	0	0	0
4/ 8/28	1018	alk	SPT	0	0	0
4/12/28	1022	ac	Tr	0	0	0
4/19/28	1023	alk	Tr	0	0	0
4/23/28	1020	ac	0	0	0	0
4/25/28	1018	ac	SPT	0	0	0
5/ 5/28	1017	ac	SPT	0	0	Rare r.b.c.
5/10/28	1018	ac	L.T.	0	0	0
5/14/28	1017	ac	SPT	0	0	0
5/17/28	1015	alk	0	0	0	Rare w.b.c.
5/25/28	1016	ac	Tr	0	0	Rare w.b.c.
5/26/28	1017	ac	Tr	0	0	Rare w.b.c.
6/ 2/28	1014	ac	SPT	0	0	Rare w.b.c.
6/ 4/28	1020	ac	L.T.	0	0	Few r.b.c.; many w.b.c.
6/ 8/28	1020	ac	Tr	0	0	0
6/14/28	1010	ac	L.T.	0	0	Rare w.b.c.
6/20/28	1011	ac	SPT	0	0	Rare r.b.c.; occ. w.b.c.
6/28/28	1014	ac	SPT	0	0	Occ. w.b.c.
7/ 9/28	1010	ac	L.T.	0	0	Numberous epithelial cells, rare r.b.c. and w.b.c.
7/21/28	1011	alk	Tr	0	0	Occ. w.b.c.
8/21/28	1014	ac	Tr	0	0	Occ. w.b.c.
8/31/28	1020	ac	Tr	0	0	Many w.b.c.
9/ 1/28	1016	ac	SPT	0	0	0
9/28/28	1011	ac	Tr	0	0	Occ. w.b.c.; 4–6 r.b.c.
10/ 9/28	1018	ac	H.T.	0	0	Rare w.b.c.
10/22/28	1014	ac	L.T.	0	0	Rare w.b.c. and r.b.c.
12/ 5/28	1020	ac	SPT	0	0	Occ. r.b.c.; rare w.b.c.

The author wishes to take this opportunity to express appreciation and thanks to Dr. William H. Robey, cardiologist, who was in frequent consultation during the course of this case, for his unselfish and helpful co-operation: also to Dr. George P. Sanborn, immunologist, and Dr. Frederick Parker, Jr., bacteriologist, for their valued participation in the treatment of this case; to all three for suggestions in the preparation of this manuscript.

CLINIC OF DR. H. ARCHIBALD NISSEN

ROBERT BRECK BRIGHAM HOSPITAL

ATONIC STASIS. CLINICAL AND LABORATORY STUDY OF INTESTINAL VARIATIONS IN CHRONIC DISEASE

THE Robert Breck Brigham Hospital in Boston, Massachusetts, has 74 charitable beds; 69 of the occupants of these beds were analyzed in this clinic. This group has been in the hospital continuously from one month to fourteen years, and their ages range from nine to seventy-two years.

The diagnoses of the sixty-nine patients are distributed in the following fashion:

Diagnoses.	Number of cases.	Diagnoses.	Number of cases.
Arthritis	44	Osteomyelitis	1
Rheumatic heart disease	10	Bronchiectasis	1
Arteriosclerosis	1	Hysteria	1
Old poliomyelitis	2	Multiple sclerosis	3
Chronic nephritis	2	Syphilis	1
Tuberculous kidney	1	Lung abscess	1
Syringomyelia	1		

The degree of helplessness is variable and fluctuant.

At the Robert Breck Brigham Hospital the personnel of the staff has been the same during the past ten years, and the patients have been under the constant observation of four of us. Daily records have been kept during this period and fairly complete laboratory studies made. Foci of infection have been removed from all of this group, except a few who have been in the hospital only a short time.

The Course of Chronic Disease.—The specific purpose of this study of chronic patients is to direct attention to the variability of intestinal activity, and to distinguish between functional and pathologic changes.

The most important fact to remember in any study of chronic disease is that the course is one of remission and relapse, of plateaus and valleys of variable duration but with a downward trend. Observations made over a period of ten years show this readily, but the usual hospitalization period of a few weeks to three months excludes all chances of watching the interesting natural curve depict itself.

This curve has a practical clinical value, in that it reveals the essential differences between chronic disease and average expectancies of life. As an example, most people know of acquaintances who have been able to carry on their daily work satisfactorily and symptom-free until a severe illness was experienced. This illness might be the carbuncle that so often attacks men in their late forties, which leaves a much deeper scar than that visible at the site of the carbuncle. This individual has lost a good deal of his vitality, interest, and activity, and he is not the man that he was before his illness, and to those who watch him for a period of years, it is clear that he never quite reaches his previous plateau of activity. Later an acute upper respiratory infection attacks him; he takes longer to recover. Apparently fully recovered, he returns to his work measurably as good as ever but functionally he is now at a lower level of activity than even after his carbuncle episode. If this man's curve of activity is plotted, it is level; up to an indefinite age he is able functionally and measurably to compete satisfactorily in the world's work, until he encounters an acute infection, disability or trauma of one sort or another. Then this curve shows a downward trend, varying in depth, followed by an upward swing due to adjustment to meet the new changes which have taken place in the body, sufficient to produce the beginning of a remission. Although he has recovered, the plateau of his curve is slightly lower than before. The individual may then continue with his work perfectly satisfactorily until extra strain is put upon him and then a relapse takes place much more quickly, taking him longer to reach the beginning of the stage of remission. After each successive setback, with or without measurable tissue change, the individual proceeds downward.

In contrast to this "normal" curve outlined above, the curve of chronic disease shows longer periods of relapse, shorter and lower plateaus of remission. The functional imbalance of the chronically sick individual is emphasized by almost weekly variations in physiology. Important among these variations are those in digestive function.

Gastro-intestinal Variations Present in Chronic Disease.—*x*-Ray studies were made this year on 53 of the 69 cases at the Robert Breck Brigham Hospital. These *x*-ray examinations showed that twenty-two of the male patients had stasis in the large intestine; six showed no stasis; twelve showed colitis. Of the females twenty-one showed stasis, ten showed none and two showed colitis. This is of particular interest when it is realized that not one of these patients had shown any of the clinical symptoms or signs of actual colitis.

In order to investigate and to interpret correctly these observations, these fourteen patients were studied more in detail. They were proctoscoped and in order to have something for comparison, twelve other patients were proctoscoped. The following are the results of these proctoscopic examinations. Not a single one of the twenty-six who were proctoscoped showed definite pathology in the rectum. It is fairly well established that colitic inflammation never localizes in one small area. It is, if present, a diffuse general lesion involving the entire colon at some time. If the *x*-ray report states localized spastic or atonic colitis of the ascending or the transverse, or a portion of the descending colon, this does not mean colitis in its pathologic interpretation, unless proctoscopic examination reveals either scarring in the rectum or a congested boggy, friable, reddened membrane, bleeding readily on slight touch. In this group of fourteen patients having a positive *x*-ray diagnosis of colitis, no actual pathology was discovered in any of the proctoscopic examinations. There were functional variations, ranging from a mucous membrane slightly irritated and granular to a normal, moist, pink membrane with no excess of mucus or adherent feces. The *x*-ray diagnosis of colitis in this group of fourteen patients with chronic disease was not confirmed by proctoscopic examina-

tion. A direct culture was obtained from the rectum of the twenty-six patients examined and on culturing nineteen showed the presence of Bacillus coli and six showed the presence of Bargen's organism; accepted by some as the etiologic cause of ulcerative colitis. Bargen's organism is described as being a small Gram-positive pleomorph arranged in diplo form. A differential diagnosis has to consider (*a*) the enterococcus which has fairly constant morphology. (*b*) The entire group of the fecal streptococci which form definite chains; (*c*) the diphtheroids which have characteristic morphology.

CASE HISTORIES—ATONIC STASIS

Comparison of *x*-Ray and Clinico-pathologic Diagnoses.—The six patients who showed Bargen's organism obtained by direct culture in September, 1928 and recultured in November, 1928 had the following histories and clinical courses. They were placed on a residueless diet outlined below in September, 1928.

Case I.—B. Arthritis. Male, age thirty-eight years. Onset 1917. A personal record made out by the patient himself is as follows: He always had excellent digestion which remained so at the onset of his illness, and at the present time he considers it to be normal. Before his illness began he was in the habit of taking Epsom salt every night. At the time his illness began his bowels were irregular and he continued his Epsom salt ingestion. He has not taken any laxatives since he entered the hospital as a patient. He has an excellent appetite and enjoys his food. He never complained of nausea or abdominal pain.

He declares that emotionally he has been discouraged, somewhat depressed and worried but he fails to appreciate any lack of functional emotional adjustment to life.

x-Ray showed a moderate amount of visceroptosis. The stomach, antrum, and duodenum seemed atonic. There was no evidence of ulcer. There was rather a marked colitis; the colon seemed very spastic.

After the discovery of the Bargen's organism, B. was placed upon a residueless dietary similar to the one developed by Alvarez and given in Cecil's "System of Medicine" and kept on this for two months. At the end of two months there was no change in his personal history except that he wanted more to eat. A second proctoscopic examination was made on November 25, 1928 and he showed a perfectly normal membrane and a normal proctoscopic examination. Direct culture, however, when planted, yielded Bargen's organism.

Case II.—D. Rheumatic heart disease. Male, age thirteen years. Admitted August 19, 1927. Onset May, 1927. His personal record: Has

always experienced excellent digestion. His bowel movements before his present illness were normal. He has never taken any laxatives. At the time his present illness began he had an enema every second day and was given laxatives. At the present time his bowels move daily and are normal, and he has not taken laxatives since his admission to the hospital. At the present time there is no abdominal discomfort, nor is there any history of abdominal discomfort in the past. Appetite has been excellent except when he had his acute rheumatic heart disease. He denies knowledge of emotional upsets of any sort.

x-Ray Diagnosis.—Stomach normal in outline with sluggish peristalsis. The first part of the duodenum spastic. It took considerable time before it

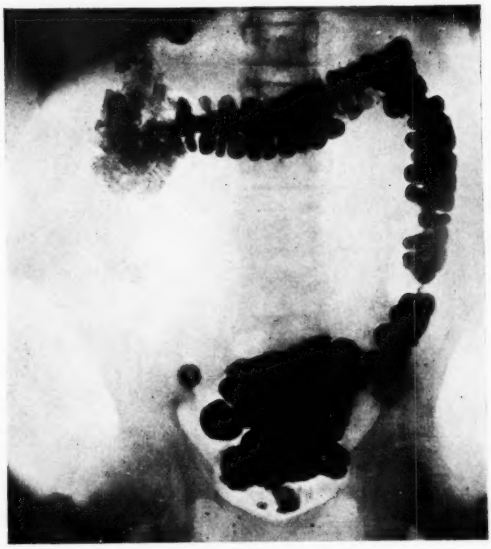

Fig. 34.—Case II.

filled, although it never filled quite satisfactorily, we believed it to be normal. At six hours no gastric residue; the head of the column had reached the head of the transverse colon. A slight amount of barium in the terminal ileum but most of it in the cecum and descending colon. In twenty-four hours it had reached the rectum but most of the barium was in the cecum and colon (Fig. 34). At forty-eight hours there was considerable barium in the transverse colon and descending colon and scybalous masses.

Conclusion.—Except for colitic stasis we would consider our examination negative.

Both first and second cultures showed Bargen's organism.

Case III.—G. Arthritis. Female, age thirty-eight years. Onset September 19, 1923. Admitted June 3, 1924. This patient has never experienced any indigestion. Previous to the onset of her illness was very constipated and took various laxatives. At the time her illness began her bowels were very irregular and she took many different laxatives and cathartics. At the present time her bowel movements are regular with the aid of cathartics. She has never had any abdominal pain or distress except nausea. Appetite has remained excellent throughout and she has a normal desire for food. She gives a perfectly definite story of emotional upsets.

Her *x*-ray plates show a horizontally placed stomach, normal in outline. Although there is a tendency of the pylorus not to round out well, it looks as

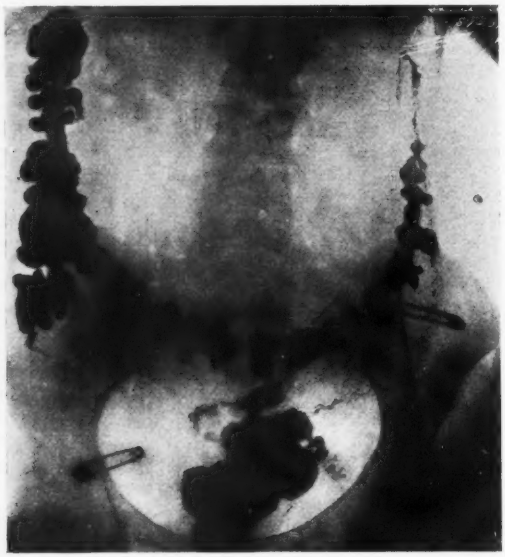

Fig. 35.—Case III.

if it was pressed down. The first part of the duodenum is spastic and it took considerable time to fill up. It never did fill up well. It looked irregular in outline and was pulled in behind the pylorus so that the picture had to be taken from an oblique angle. At six hours there was no gastric residue; the head of the column had reached the hepatic flexure. The appendix was seen and was attenuated and the tip overhung the brim of the true pelvis. At twenty-four hours most of the barium was still in the cecum and the column had reached the rectum (Fig. 35). At forty-eight hours a trace of the barium was seen in the cecum, the descending colon, and the rectum. The transverse colon is of the hammock type and the last portion is at the brim of the pelvis.

Although no gall-bladder plates were taken there were several shadows seen in the stomach plates that looked as if there might be small calculi. Except for chronic stasis of the transverse colon, examination was negative.

Case IV.—K. Arthritis. Female. Onset August, 1926. Admitted October, 1927. Age sixty-three years. Patient declares she has never had indigestion of any sort. Previous to the onset of her present illness she took cascara occasionally. At the present time she is taking small quantities of American oil at night and one alophen tablet. She has never complained of

Fig. 36.—Case IV.

abdominal discomfort or pain; never has had nausea and appetite has always been excellent. No personal appreciation of any emotional disturbance.

x-Ray examination showed forty-eight-hour stasis (Fig. 36).

Bargen's organisms were grown from both cultures.

Case V.—K. Boy, age thirteen years. Rheumatic heart disease. Onset 1923. Admitted September, 1927. Patient denies ever experiencing any indigestion. Bowel movements have been normal and regular, occasionally he takes a laxative. At no time has there been nausea, abdominal distress, and except for a short period during the acute rheumatic fever has had ex-

cellent appetite and a normal desire for food. Patient denies any emotional upsets.

x-Ray Report.—Stomach in normal position, regular in outline, normal tone and peristaltic activity. Antrum spastic. First part of duodenum filled and emptied. Second and third part of duodenum showed some delay. At six hours stomach was empty and the head of the column had reached the hepatic flexure. Slight delay in the terminal ileum. Appendix not seen. Twenty-four-hour examination showed that the head of the column had reached the rectum. Cecum and ascending colon emptied normally. Transverse colon spastic. At the end of forty-eight hours there was slight trace of barium in the lower part of the cecum. There was considerable barium in the rectum with a trace of it scattered through the colon. No fixed areas or definite deformities noted.

Conclusion.—Esophagus, stomach, antrum, and first part of duodenum negative. Moderate amount of stasis in the large intestine, especially in the rectum. A moderate degree of spastic colitis especially involving the transverse colon.

On November 25th proctoscopic examination showed a normal, pink membrane with no excess mucus and no feces. Bargen's organisms were obtained from the first but not the second culture.

Case VI.—C. Arthritis. Male, age twenty-eight years. Onset 1919. Admitted October, 1921. This patient gives a story of having had an occasional attack of heart-burn and slight indigestion previous to the onset of present illness. Before his present illness his bowel movements were regular but he averaged two alophen pills a week. At the onset he was inclined to be irregular in bowel activity but for the past year has not taken any laxatives and bowel evacuations have been regular and normal. There has been an occasional definite change in desire for food, complaining at times of anorexia. There has been no pain, nausea nor abdominal discomfort at any time. His emotional history from his point of view is negative.

x-Ray of esophagus negative. Stomach rather low, long, and slightly atonic, regular in outline. Peristalsis normal. There was a good antrum. Sphincter and first part of the duodenum seen. Duodenum slightly spastic. Just a trace of barium in the stomach at the end of six hours. The head of the column was in the hepatic flexure. At twenty-four hours it had reached the rectum. At forty-eight hours there was considerable barium scattered throughout the colon with a fair amount in the rectum. The cecum was low and distended at the end of twenty-four hours. In forty-eight hours it had fairly well emptied. The cecum appeared atonic. There was considerable delay in the terminal ileum at the end of six hours. The entire colon seemed spastic. No tender points or deformities noted in the colon.

Conclusion.—The esophagus, stomach, antrum, and first part of the duodenum appeared normal. The stomach seemed atonic and there was a very small six-hour residue. There was marked stasis in the ileum and in the cecum at the end of twenty-four hours. The cecum was low and dilated with a trace of barium in the ileum. The cecum was movable but not tender. There was a moderate degree of stasis throughout the entire colon at forty-

eight hours, most marked in the rectum. Rather marked degree of spastic colitis.

Proctoscopic examination repeated on November 25th showed normal mucous membrane, no blood or mucus. Bargen's organisms obtained at the first proctoscopy but not at second.

The residueless colitic diet mentioned is as follows:

Breakfast:

Orange juice, grapefruit (avoid the fiber), cantaloupes, and melons are inadvisable as they tend to regurgitate. One or two eggs with ham or bacon (avoid the purely fibrous part). Coffee in moderation, cocoa, chocolate or tea.

White bread and butter; zwieback or toast.

Any smooth mush such as farina, germea, cream of wheat, cornmeal, or strained rolled oats. Puffed cereals and corn flakes are also allowed. Shredded wheat biscuit and other coarse breakfast foods are not allowed.

Lunch or Dinner:

Broths, bouillon, cream soups, chowder.

Small portions of meat, fish, oysters, chicken, or squab. No smoked or canned fish or pork. Avoid veal, crab, lobster if they seem to cause indigestion.

White bread and butter, hot biscuits made small so as to consist mainly of crust. No rough bran bread or biscuit.

Rice; potatoes, baked, mashed, browned or French-fried. Sweet potatoes, hominy; tomatoes stewed, strained, and with cracker crumbs. Well-cooked cauliflower tops with cream sauce, and asparagus tops. Later may try Brussell sprouts. Italian pastes, noodles, macaroni, spaghetti, cooked soft with a little cheese or cream sauce. Purées of peas, beans, lentils, lima beans, or artichokes. All skins or fiber should be removed by passing through a sieve. "Kornlet" in cans furnishes sweet corn without the indigestible husks. There are practically no other vegetables that can be puréed to an advantage. Spinach often causes trouble and is not recommended. Bananas can be fried in butter or baked in their skins. String beans are allowed if young and tender. No salads at first, later you may try a little tender lettuce with apples or tomato jelly, bananas, or boiled egg. Mayonnaise and French dressing are allowed.

For Dessert:

Simple puddings, custard, rice, jello, plain cake, canned or stewed fruit. Avoid cheese, nuts, raisins.

The interesting feature of this residueless diet for colitis is that there is a very markedly deficient intake from a mineral and vitamin point of view; also it is very high in starch and sugar, very low in fat and low in protein. In fact I do not believe that it is practical to keep a patient strictly on this diet for a period

exceeding three weeks as a rule, because of its mineral and vitamin deficiency, and its marked imbalance of carbohydrates, fat, and protein.

The six patients of the Robert Breck Brigham Hospital showed interesting reactions to this diet. They were taking the diet with cod-liver oil and vegex or vitavose, without, however, the orange juice or lemon juice for over two months. At the end of this time there was a decided measurable change in the tone of the tissues and some increased joint irritation among the arthritics in spite of the fact that there has not been recorded any so-called "digestive upset" or any "acute attack of colitis." As a matter of interest, not one of these patients has ever had an acute colitic upset.

The bedridden or the so-called "chronic" patient, the undernourished or partly demineralized patient if watched over a period of years will show by serial gastro-intestinal *x*-ray studies, depending upon the degree of inactivity and gradual progression, loss of tone of the intestinal tract. This continues until haustral markings are lost, the colon becomes smoothed out and atonic. There may be regions where there is spasm, more often there is an atonic generalized condition present. If there is no change in the dietary and the patient is kept in bed without exercise and given the usual hospital diet after the loss of normal intestinal markings and the loss of tone, stasis develops. Then usually follow laxatives, cathartics, and enemas; and then not uncommonly there is developed an excess of mucus, foul stools, soft and formless or scybalous masses. Not infrequently this picture progresses to one where there are actually stools with or without varying amounts of pus due to localized trauma. Any patient complaining of bleeding from the rectum or of lower abdominal discomfort should have proctoscopic and digital and *x*-ray examinations because of the insidious nature of cancer.

At this stage the proctoscopic examination is negative, as are direct cultures. If the patient is placed on a regular régime of daily exercise, which may be the simplest of exercise or rather complicated, but at any rate sufficient to produce better circulation, and a fairly general exercise of muscle function and more

roughage is added to the diet with mineral oil in small doses added also, it is remarkable how often what from the *x*-ray point of view is termed "colitis" will clear up. Also it is not unusual, depending upon the age and duration of the loss of tone, to see how rapidly and completely some of these intestines become restored to their normal picture. This is obviously not the picture we describe as ulcerative colitis.

The above picture which includes the first six patients described I believe should be termed "atonic stasis of the colon" with resulting obstipation but never true ulcerative colitis because of the negative proctoscopic examinations and clinical courses.

The patient's history should be obtained in as complete detail as is possible. After such a history has been obtained a physical examination should be made, examining the patient from head to foot. Proctoscopic examinations should be made if there is an intestinal history, and Bargen's organism may or may not be obtained. The serial *x*-ray pictures of the gastro-intestinal tract are indicated and I believe should be done once a year. The usual laboratory procedures should be carried out.

When the above measures have been done one is still far removed from actually knowing his patient, because the patient has a conscious make-up and an instinctive make-up. This is certainly discernible in a hospital like the Robert Breck Brigham where the same patients are observed year in and year out, to a certain extent are retired from the business of living, not having earned their retirement. Consciously they wish to improve, they wish to become well and normal; instinctively, however, they do not. If one watches them, one finds that what they say and what their actions tell you are two different things. They are protected; they have everything done for them; they have a roof over their heads and have a bed; they have food, entertainment, occupation, medical care, and they have no responsibilities. Instinctively they have achieved the goal most humans work for and accomplish in varying degrees of success.

Some of these patients can be made to become interested enough so that even with a degree of measurable functional impairment, they can leave the hospital and earn their own living

in a competitive world. They can live upon a slightly lower scale of functional activity than previously if they adapt themselves whole heartedly to this adjustment, and will continue to function and live more comfortably because of a better understanding between their conscious and instinctive elements. They will have gained more than those who remain in the hospital as chronic invalids.

Summary.—Regular routine observation of chronic disease patients for a number of years show that they present symptoms and signs from time to time that cannot be interpreted correctly if the usual methods of acute disease are applied. These chronic patients develop a physiology peculiarly their own and different from that usually accepted.

The gastro-intestinal tract shows variations which are consistent from an *x*-ray viewpoint with pathology but not from the clinical side. The origin, course, and result of these variations in the gastro-intestinal tracts of chronic patients are explained upon a functional basis. The constant presence of the emotional side in all its subtle manifestations is as important in chronic disease as in any type.

If patients with chronic disease are *x*-rayed serially the gastro-intestinal tract shows increasing atonic stasis. This is mistermed "colitis." It is not colitis because no other proof of colitis has been found except the *x*-ray diagnosis. This has led to confusion in diagnosis and treatment.

Bargen's organism is accepted by some as the cause of ulcerative colitis. It was present in direct culture in six of the fourteen patients diagnosed colitis. But no colitis has been detected by proctoscopic examination or clinical course.

The observations noted in this presentation are offered for what they represent, namely, some interesting but commonly misinterpreted aspects present in chronic disease.